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ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
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BRONCHIECTASIS—DEXTROCARDIA—SINUSITIS

A contribution to the aetiology of bronchiectasis

by

Carl E. Gudbjerg

Although bronchiectasis has been known as a well-defined disease entity for more than a century, its aetiology and pathogenesis have been the subject of long-standing discussion in which opinions have been, and still are, rather divergent. Radiologic studies, especially bronchographic serial examinations, have been of great importance in the investigation into the exact nature of the disease, but have so far been unable to provide a satisfactory explanation of its origin.

The classical main division of bronchiectasis is that it may either be congenital or acquired.

On the basis of radiologic, clinical and experimental studies the development of acquired bronchiectasis is explained by complete or partial bronchial obstruction by a foreign body, a tumour or inflammatory products, which in turn causes a retention of bronchial secretion. Owing to secondary infection, chronic inflammatory reactions develop in the bronchial wall, which is weakened. The increase in the intrabronchial pressure produced by cough will then give rise to dilatation of the bronchi.

FLEISCHNER (1949) expressed the view that atelectasis is the primary disease and is, alone, capable of producing dilatation of the bronchi, whereas TANNENBERG and PINNER (1942) regarded infection as the primary condition and concluded thus: "A comparison of the experimental observations with the changes seen in human pathology makes it more probable that uncomplicated atelectasis per se has no bearing whatever on the development of bronchiectasis. There is, however, another rela-

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From the Departement of Radiology (Director: Professor: P. Flemming Moller), University Hospital, Copenhagen, Denmark.

tionship of these two conditions. Both may be produced by the same cause. Atelectasis in children and other primary diseases which are found frequently in the history of bronchiectasis are caused almost without exceptions by inflammatory conditions in the lung. Bronchial exudate and inflammatory swelling of the bronchial mucosa may close the bronchial lumen and cause atelectasis within a short time."

Owing to the anatomic relationship, compression by surrounding lymph nodes may especially involve the right middle lobe, in which bronchial occlusion may be caused by only moderate enlargement of the nodes. This gives rise to the so-called middle lobe syndrome. Due to impaired bronchial drainage, the middle lobe becomes swollen and consolidated, and after the resolution of the acute process the bronchial ramifications will often be dilated.

Traction from the surrounding pulmonary tissue may no doubt accelerate the development of bronchial dilatations and may probably also give rise to ectasia independently. This aetiology plays a special rôle, for example, in fibroid tuberculosis. Such cases of bronchiectasis are most frequently localized to the upper lobes and are not very rare.

According to SAUERBRUCH (1929), most cases of bronchiectasis are congenital and caused by a developmental defect of the bronchial wall.

DIAMOND and VAN LOON (1942) voiced the opinion that if bronchiectasis has no congenital basis but is due to injury to the bronchial wall caused by inflammatory changes, the factors which operate to produce ectasia are not effective in all cases. The authors arrived at this conclusion from a study of 150 children with entirely uniform clinical manifestations, although one half of the patients had bronchiectasis, while the remaining half showed perfectly normal bronchograms.

DAVISON (1944) suggested that allergy may be an aetiologic factor both in bronchiectasis and in a frequently co-existent sinusitis.

That bronchiectasis has often been claimed to be of congenital origin, is due, inter alia, to the observation that the disease is strikingly often associated with changes which are definitely referable to developmental anomalies.

SIEWERT (1903) was the first to describe a case of situs inversus organorum with concurrent bronchiectasis; the possibility of a relationship between these diseases, however, was first suggested by KARTAGENER (1933), who also stated that chronic sinusitis and defective development of the frontal sinuses belonged to the disease complex which has since borne the name of Kartagener's triad. According to KARTAGENER, the frequency of bronchiectasis in dextrocardia was 25 per cent.

ADAMS and CHURCHILL (1937) reported a figure of the same order of magnitude, while OLSEN (1943), who collected 85 cases of dextrocardia, demonstrated bronchiectasis in 14 instances, or 16.5 per cent.

BERGSTRÖM et coll. (1950) surveyed a total of 82 cases of Kartagener's triad published up to that time and stated that bronchiectasis was found in 12 to 23 per cent of cases with situs inversus. Since that time a few cases of the syndrome have been published, inter alios, by BLIXENKRONE-MØLLER (1950) and by ZUCKERMAN and WURTZEBACH (1951).

BANHAM (1950) reported a similar case in a man, aged 44, in whom defective development of all the air sinuses was accompanied by a considerable degree of lack of pneumatization of the temporal bones.

In addition to being part of Kartagener's triad, inflammatory changes in the paranasal air sinuses are also a phenomenon frequently accompanying acquired bronchiectasis. However, it is not quite clear if the inflammation is the primary complaint and thus the cause of the bronchial dilatation, or if it develops secondary to the infection of the respiratory tract.

According to HOGG and BROCK (1951), various investigators have reported the following frequencies of sinusitis in bronchiectasis:

CLERF (1934)	82.4 %
WATKINS (1936)	89.3 %
ORMEROD (1941)	42.5 %
HOGG (1951)	60.9 %

KARTAGENER reported a frequency of situs inversus of 1 : 5,000 at autopsies, while ADAMS and CHURCHILL found an incidence of 1 : 10,099 at clinical examinations. In routine examinations of a total of 114,130 individuals among army personnel, EHRLICH et coll. (1943) found 54 cases of bronchiectasis, subsequently confirmed by bronchography. This corresponds to a frequency of 1 : 2,150 in the general population.

Personal Investigations

Dextrocardia. During the period 1941—1953 a total of 25 cases of dextrocardia were diagnosed at the Department of Radiology of the University Hospital, Copenhagen. In thirteen of the cases there was coexistent transposition of the abdominal viscera, while twelve had dextrocardia only. In six patients, the anomaly was complicated by congenital cardiac disease. Otherwise, the transposition of the viscera was not accompanied by additional malformations.

Of these patients, nine were women and sixteen men. The average age for the former was 28 years and for the latter 16 years. The oldest female patient was 64 years and the youngest 2 years at the time of the diagnosis, the corresponding ages for the male patients being 65 years and 1 month. The age distribution is shown in Table 1.

Table 1

Age distribution of 25 patients with dextrocardia

	Age, in years					Total
	Under 6	6—10	11—20	21—30	Over 30	
No. of patients	9	2	2	6	6	25

One patient, a woman, aged 54, complained of a tendency to mild, unproductive cough during winter, but the chest roentgenogram showed normal conditions, and there were no clinical signs of bronchiectasis.

In a man, aged 61, the chest roentgenogram revealed old pleural changes with obliteration of both phrenicocostal sinuses, but otherwise normal appearances. Clinical signs of bronchiectasis were not revealed.

A woman, aged 29, had small scattered calcifications in one lung suggesting old tuberculosis. The chest roentgenogram was otherwise normal and the patient showed no clinical manifestations of bronchiectasis. In three of the six patients with complicating congenital cardiac disease increased pulmonary markings suggested mild congestion, while the remaining 19 patients showed perfectly normal chest roentgenograms, and none of these 22 patients disclosed any clinical evidence of bronchiectasis.

Owing to absence of indications, these patients were not subjected to bronchographic examination, but in view of the roentgenographic appearance of the lungs and the absence of clinical manifestations, there may be justification in saying that dextrocardia was not associated with bronchiectasis in any of these instances.

According to the calculations of the investigators mentioned, it would have been expected that at least 4 to 5 of the patients would have had pronounced bronchiectatic changes.

Even though the present series is too small to allow of any definite conclusions, it may nevertheless be questioned whether the association between dextrocardia and bronchiectasis is quite as intimate and common as has previously been supposed.

Sinusitis. During the period 1946—1953 more than 100 cases of bronchiectasis verified by bronchography were diagnosed at the Department of Radiology of the University Hospital, Copenhagen. Simultaneous roentgen examinations of the air sinuses were made in 35 of these patients and, of these, 30 were examined by an otolaryngologist. In the remaining cases there were no indications for such examinations. The case material is thus partially selected, and the occurrence of sinusitis in association

with bronchiectasis must therefore be regarded as considerably less frequent than suggested by the results of these examinations.

Only a few of the patients were studied by cutaneous tests and counts of eosinophil leukocytes with a view to allergy. Neither these studies nor the past histories of the patients were suggestive of the presence of allergic reactions.

The sex and age distribution of the patients appears from Table 2.

Table 2

Age and sex distribution of 35 patients with bronchiectasis examined for sinusitis

	Age, in years					Total
	Under 11	11—20	21—30	31—40	Over 40	
Males, normal air sinuses	0	1	1	4	12	18
Females, normal air sinuses	0	0	1	1	5	7
Males with sinusitis	1	0	1	3	2	7
Females with sinusitis	0	0	1	0	2	3

It is seen that 25 of the 35 patients showed no evidence of sinusitis. However, in 3, the roentgenograms revealed a doubtful blurring of the sinuses, but at a subsequent examination at the Department of Otolaryngology no affections of the accessory sinuses could be demonstrated, and the fluid used for lavage after a diagnostic puncture was perfectly clear. In the remaining 22 patients, there was good agreement between the roentgenographic appearance and the results of the otolaryngologic examination.

Among the 10 patients with sinusitis, only the maxillary sinuses were involved in two cases, while the remaining eight were suffering from pansinusitis. In all 10 patients there was complete agreement between the roentgenographic appearances and the otolaryngologic examination.

In view of previously reported results, it is rather surprising that only 28.6 per cent of the patients showed signs of inflammation of the air sinuses. Moreover, as already pointed out, these patients represented a selected case material, for which reason it must be supposed that scarcely more than about one-fifth of all cases of bronchiectasis are complicated by sinusitis. The results of the study suggest that sinusitis must be regarded as a sequela of bronchiectasis, which occurs because infected material from the bronchi gains entrance to the sinuses. There seems to be no evidence in support of the assumption that sinusitis is an aetiologic factor in the development of bronchial dilatation.

Discussion and Conclusions

Experimental studies have shown that it is possible to produce bronchiectasis *in vivo*.

WARNER and GRAHAM (1933) inserted a balloon into the bronchus of one of the lower lobes of the lungs of anaesthetized dogs. The baloon was inflated. The dogs were then allowed to come out of the anaesthesia and, in the majority of cases, showed few signs of respiratory distress. Roentgenograms taken 24 hours later showed a triangular atelectasis in the lower lobe, displacement of the mediastinum, and elevation of the diaphragm, *i. e.* the same picture, which may be found in bronchiectasis of the lower lobe.

Bronchographic serial examinations have unquestionably established the existence of acquired bronchiectasis. On the other hand, direct evidence has never been produced to show that congenital bronchiectasis exists, nor have definite hereditary factors been demonstrated in the aetiology.

The clinical picture of acquired bronchiectasis is well known and characteristic. The bronchographic changes most frequently consist in cylindrical, less frequently in purely saccular, dilatations of the bronchi. Occasionally, both cylindrical and saccular dilatations are observed. The disease is most common in the lower lobes, the right middle lobe and the lingula of the left lung. The signs and situation of the so-called congenital variety do not differ in any way from those in the acquired form. The histologic picture is the same in both forms, and cylindrical dilatations are also the most common in cases usually described as congenital.

The age at which bronchiectasis was diagnosed for the first time was determined by an analysis of the hospital records. From Table 3 it appears that in 19, or 61 per cent, of 31 non-selected patients with Kartagener's triad the disease was not demonstrated until after the age of 20 years. The youngest patient was 3 years, the oldest 58 years, the average age being 22 years. This figure seems strikingly high for a congenital disease. It is well known that acquired bronchiectasis may occur even in early infancy in atelectatic segments of the lungs.

Table 3

Age distribution of 31 patients with Kartagener's triad

	Age, in years					Total
	Under 6	6—10	11—20	21—30	Over 40	
No. of patients.....	1	5	6	12	7	31

FINDLEY (1933) pointed out that such dilatations may be reversible and disappear after re-expansion of the atelectatic segments.

Even though it would be difficult to produce direct evidence in support of the assumption, it is nevertheless conceivable that bronchiectasis may be acquired during late intra-uterine life, for example, after aspiration of amniotic fluid during delivery.

As long as no definite proof is available, there would appear to be no justification in maintaining the theory of a congenital origin of bronchiectasis, which in this connexion does not include congenital cystic disease of the lung.

But how is it then possible to explain the frequent association between such an unquestionably congenital developmental abnormality as dextrocardia and bronchiectasis? A possible explanation is that the transposition of the heart and the vessels might to some extent impair the circulation and thus predispose to atelectasis and infection due to oedema and congestion.

On this presupposition it is likely that prophylactic therapy directed towards respiratory infections might be conducive to decreasing the frequency of bronchiectasis in patients with dextrocardia.

SUMMARY

From clinical, radiologic and experimental studies it is concluded that bronchiectasis is, in all probability, invariably acquired.

Obstruction and infection are considered to be the most common causes of the disease, but compression by enlarged lymph nodes and traction from surrounding pulmonary tissue may also produce bronchial dilatations. Definite hereditary factors have never been demonstrated. In 25 patients with dextrocardia not a single case of bronchiectasis was found. Among 35 patients with bronchiectasis confirmed by bronchography, sinusitis was demonstrated in 28.6 per cent by combined radiologic and otolaryngologic examinations.

ZUSAMMENFASSUNG

Aus klinischen, röntgenologischen und experimentellen Studien geht hervor, dass Bronchiektasien aller Wahrscheinlichkeit nach stets erworben sind. Obstruktion und Infektion werden als die gewöhnlichsten Ursachen dieser Erkrankung angesehen; Kompression durch vergrösserte Lymphknoten und Traktion vom umgebenden Lungengewebe kann jedoch ebenfalls Erweiterungen der Bronchien erzeugen. Bestimmte hereditäre Faktoren sind nie nachgewiesen worden. Bei 25 Patienten mit Dextrokardie wurde kein einziger Bronchiektasiebefund erhoben. Unter 35 Patienten mit bronchographisch bestätigten Bronchiektasien wurde bei 28.6 % der Patienten durch kombinierte radiologische und otolaryngologische Untersuchungen eine Sinusitis nachgewiesen.

RÉSUMÉ

Des travaux cliniques, radiologiques et expérimentaux amènent à conclure que les bronchiectasies sont, selon toute probabilité, toujours acquises.

L'obstruction et l'infection sont considérées comme les causes les plus fréquentes, mais la compression par des adénomégalies et la traction par le tissu pulmonaire environnant peuvent aussi donner lieu à des dilatations bronchiques. L'existence de facteurs héréditaires précis n'a jamais été démontrée. Sur 25 sujets atteints de dextrocardie l'auteur n'a pas trouvé un seul cas de bronchiectasie. Chez 35 malades atteints de bronchiectasies confirmées par la bronchographie, les examens radiologiques et oto-rhino-laryngologiques combinés ont mis en évidence une sinusite dans 28.6 pour cent des cas.

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THE TECHNIQUE OF ASCENDING PHLEBOGRAPHY OF THE LOWER EXTREMITY

by

Torgny Greitz

The credit for having first introduced phlebography as a method of studying the deep veins is due to BERBERICH and HIRSCH (1923), who made use of an aqueous solution of strontium bromide, and to DOS SANTOS (1938), who used Perabrodil as the contrast medium. These pioneers carried out phlebography with the patient in a dorsal position during the injection and subsequent exposures. It appears to have been known at an early date that the technical difficulties in phlebography are far greater than in arteriography, as there may be incomplete filling of the veins due to the injection of the contrast medium being made in one of several peripheral branches. In arteriography, however, injection into a central trunk results in the contrast medium mixing immediately with the blood and being carried on through all the branches. Other technical difficulties have also to be taken into account; of essential importance to the development of the technique of phlebography has been the statement made by LINDBLOM (1941) that, when phlebography is carried out with the extremity horizontal, the contrast medium fills only the lower portion of the lumen of the veins — often as a thin streak — which gives a misconception of the real anatomy. According to LINDBLOM this is due to sedimentation of the contrast fluid. However, RIBBING in his works on the source of errors in pyelography has pointed out that sedimentation is the sinking of solid particles through a liquid. If one liquid lies unmixed on top of another this is referred to as layer formation and is usually due to a difference in their specific weights. The expression 'sedimentation' is, however, still used, and in many quarters the misconception still prevails that the water-soluble contrast media (Umbradil, diodone, etc.) sink to the bottom after they once are mixed with blood.

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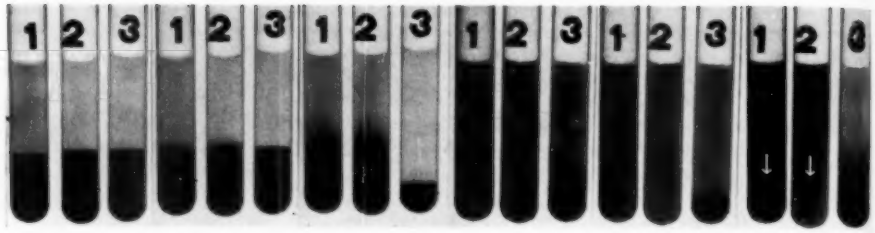


Fig. 1. The difference between sedimentation and layer formation.
a. Citrated blood in layers over Umbradil 25 % (tube 1), Umbradil with dextran (tube 2) and barium sulfate of the same density as that of Umbradil 25 % (tube 3). Immediate film.
b. After 15 minutes; the water soluble Umbradil has begun to diffuse into the blood.
c. After 7 hours; the division between the blood and Umbradil in tubes 1 and 2 has been obliterated by diffusion, while the barium sulfate has descended to the bottom, forming a sediment.
d. Immediately after shaking the ingredients, the barium sulfate has already begun to settle. No change in the blood-Umbradil mixture.
e. Two minutes after shaking. Note the sedimentation in tube 3.
f. Four days later; the blood corpuscles in tubes 1 and 2 have sunk to the bottom and formed a sediment with a sharp upper outline (↓↓).

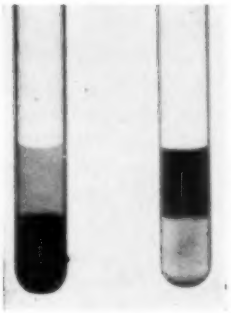


Fig. 2. Heparin, blood, and Umbradil of the same specific weight, poured into tubes in layers. The tube on the left contains blood over contrast medium, the right, contrast medium over blood.

This is not the case which a simple experiment (Fig. 1) illustrates. Even two liquids of the same specific weight may be held in two separate layers one above the other with a sharp line of demarcation provided one of them has such a high rate of viscosity that no mixing takes place at the boundary layer. This is the case with blood and Umbradil of the same specific weight (Fig. 2).

To eliminate the source of errors caused by the layering, LINDBLOM has suggested that phlebography should be carried out with the extremity in a vertical instead of a horizontal position. It seems as though LINDBLOM's work has not always been appreciated, phlebography still being carried out in many quarters with the patient in the dorsal position. Objections have even been raised against the 'vertical technique' (BAUER 1945, 1947, 1951). The technique of phlebography is also very much in dispute in other respects. If, for example, one

studies HÖJENSGÅRD's monograph (1951), one will find that practically every technical detail still remains a subject for discussion. The present article is an attempt to throw some light on this discussion and present a simple method based upon theoretical, experimental, and purely practical foundations.

Experiments have been carried out *in vitro* to investigate the layer formation of blood and contrast media. In addition, nearly 200 patients have been examined in such a way that, on one and the same visit, phlebography has been carried out twice on the same leg with a varying technique. The technique has only been varied by changing one factor at a time (for example: first a short, then a long period of injection). This method of examination will hereafter be referred to as a double examination (d. exam.). The intention is to afford answers to a number of questions discussed in the matter which follows. The examinations have been performed on patients with chronic venous insufficiency; none have been made on normal cases, since it is not at all certain that a given technique suitable under normal conditions is the best one in pathologic conditions. To find out to what extent conclusions may be drawn from d. exam., phlebography on 10 patients in the erect position has twice been carried out with exactly the same technique at each examination. In 9 cases the results were identical. In one case, a slightly inferior density of the contrast medium was obtained in the thigh and pelvis, possibly due to a decrease in blood pressure which had passed unobserved. Hypostasis caused by threatening syncope reduces the circulation time, thus causing the contrast filling to decrease proximally. If a patient faints during an examination the contrast medium may remain in the lower leg and not continue on into the thigh, whereas this will not occur if the examination is repeated when the patient exhibits no tendency to faint (Fig. 3). However, an increase in the blood pressure in a patient with no tendency of fainting, produced by giving ephedrine, did not improve the contrast filling. No difference could be observed in this respect in examinations made on patients with normal blood pressure or with hypertonia. This has been shown by comparing the phlebograms of a group of 35 patients whose blood pressure was less than 150 mm Hg with a similar group in which the blood pressure was 150 or more. There also does not appear to be any relation between the velocity of the circulation in the veins and the arterial blood pressure. During phlebography on a patient in the erect posture, the rate of the contrast stream varies considerably and indirectly gives a fairly good idea of the rate of the circulation. In the case of patients with rapid venous circulation, the lower part of the leg and thigh will quickly be emptied of contrast medium and very good filling of the veins of the pelvis obtained. In the case of patients with slow circulation the contrast medium will remain for a long time in the

lower leg and the filling of the pelvic veins be retarded, often to an unsatisfactory extent. As the optimal time for the contrast filling of the pelvic veins is thus very variable, it is advisable to make more exposures of the pelvis than of the thigh and lower part of the leg. An additional factor is that the optimal filling of the pelvic veins with contrast medium only lasts for a short while. Two films taken at different examinations must therefore have been exposed at exactly the same interval after the conclusion of the injection to be comparable. Even a slight variation in the time of exposure or an attack of fainting on the part of the patient — difficult to control — may thus influence the result. Care must be taken that the films are exposed at the same intervals in both examinations, and that the patient shows no tendency to faint. These conditions have been carefully observed in the examinations which form the foundations of the following discussion.

The questions now to be raised concern the position of the extremity during the examination, the character and amount of the contrast fluid, the method of injection and the measures taken to improve the contrast

a. b.

Fig. 3. a. Patient fainted during the examination, which was carried out in the vertical position. Contrast medium remains in the lower leg and there is practically no filling of the thigh vessels.

b. Same patient and same technique after injection of ephedrine. No tendency to faint. Satisfactory contrast-filling of the popliteal and femoral veins.

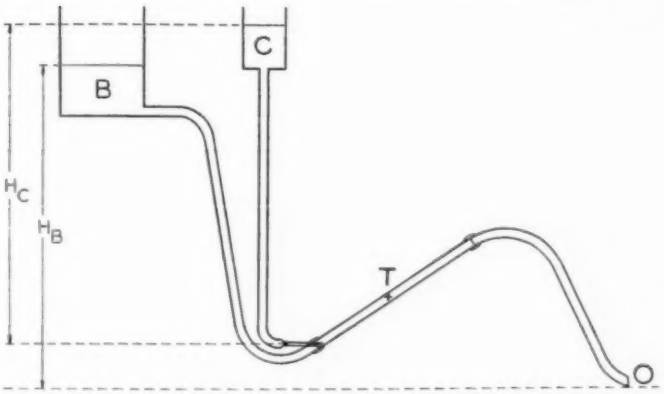


Fig. 4. Experimental arrangement for studying the blood-contrast system flowing in vitro. B = container with citrated blood. C = container with contrast medium (Umbradil 35 %). T = glass tube in which layer formation may be studied roentgenologically; the tube can be rotated around the axis X. O = outlet for blood-contrast. H_B = the height of fall of the blood when flowing from B to O. H_C = the height of fall of the contrast medium while flowing from C to the tube.

filling in the deep veins through compression, movements of the muscles, etc.

The question if phlebography should be carried out with the leg vertical or horizontal has earlier been considered by LINDBLOM, KJELLBERG, LÖFSTEDT and others. LINDBLOM (1941) stated that the deep veins in normal cases may fail to fill if phlebography is carried out with the leg supine; the contrast will then follow the superficial veins on the dorsum of the limb. The basis of this phenomenon is, as mentioned above, the disinclination of the contrast medium to mix with the blood, and its high specific weight which results in layer formation between the two fluids. This has been experimentally studied by KJELLBERG, who has examined serum and a contrast medium flowing together through a glass tube. He writes: "Obwohl der Winkel zur Horizontalebene mehr und mehr vergrössert wird kann man keine Veränderung im Aussehen der Kontrastmittelmasse feststellen." However, if KJELLBERG's films are studied, it will be noted that the relationship between the thicknesses of the layers of contrast medium and serum varies if the angle to the horizontal plane is varied. To give a clearer picture of this condition the author has employed the following experimental arrangement (Fig. 4.)

Citrated blood is carried via a rubber tube from a container (B) through a glass tube (T) into which a contrast medium (Umbradil 35 %) is injected from another container (C). A roentgenologic record of the flow is obtained by films taken with the rays

directed horizontally. If the tube (T) is in a horizontal position, and the height of delivery (H_B) constant at the beginning of the experiment, the thickness of the layer of contrast medium will increase if the pressure of the injection is raised by increasing the height of the column of contrast medium (H_C). If H_C is kept constant, and H_B successively increased, the layer of contrast medium will become thinner and thinner. If H_B is decreased the layer of contrast medium will become thicker. If H_C and H_B are kept constant while the slope of the tube is varied, the thickness of the layer of contrast medium will alter, although the rate of the circulation of the blood is constant the whole time. This can be controlled by determining the blood flow before the injection of the contrast medium. If the tube is placed horizontally the formation of the layer may be clearly seen. If the distal end is successively raised, the thickness of the layer of contrast medium increases. If it is successively lowered the contrast medium will eventually only flow through the tube in a thin streak (Fig. 5). This may also be studied in vivo (Fig. 6).

It should be especially noted that the 'layers' are most pronounced in extremities examined in the vertical position when the flow of blood is directed downwards. It is therefore not enough to state that phlebography should be carried out with the extremity in a vertical position, but more fully and correctly: ". . . the extremity in a vertical position with the flow of blood directed upwards." That the layer of contrast medium becomes thinner when flowing 'downhill', and comparatively thicker when proceeding 'uphill' may also be seen from several other experiments (Fig. 7 a, b, c). It is, however, not always ceratin that the contrast medium will follow the inferior wall of a vessel. KJELLBERG has observed that at a curve in the vessel may be noted "wie sich der Kontrastmittelstrom in zwei Teile verzweigt, deren eine kleineren weiterhin der Gefässboden folgt während die Hauptmasse des Kontrastmittels in weiten Bogen durch den Serumstrom hindurch nach der gegenüberliegenden Wand geschleudert . . . wird". The present writ-

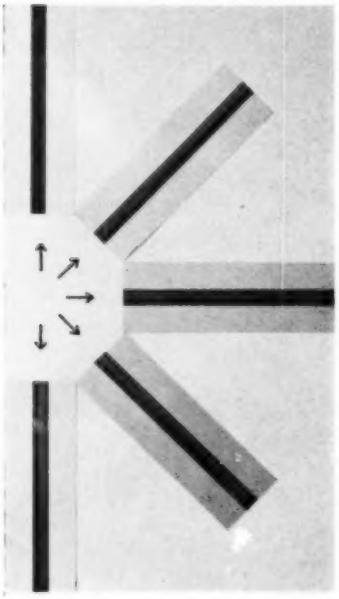


Fig. 5. Variations in the thickness of the layer of contrast medium due to the angle of the incline, studied with the experimental arrangement shown in Fig. 4. The arrows indicate the direction of the flow. In a vertical tube with the blood stream directed upwards, the contrast medium distributes itself over the whole lumen. If the tube is inclined the contrast medium will follow the inferior wall; the more the distal (right) end of the tube is lowered, the thinner the contrast layer will become.

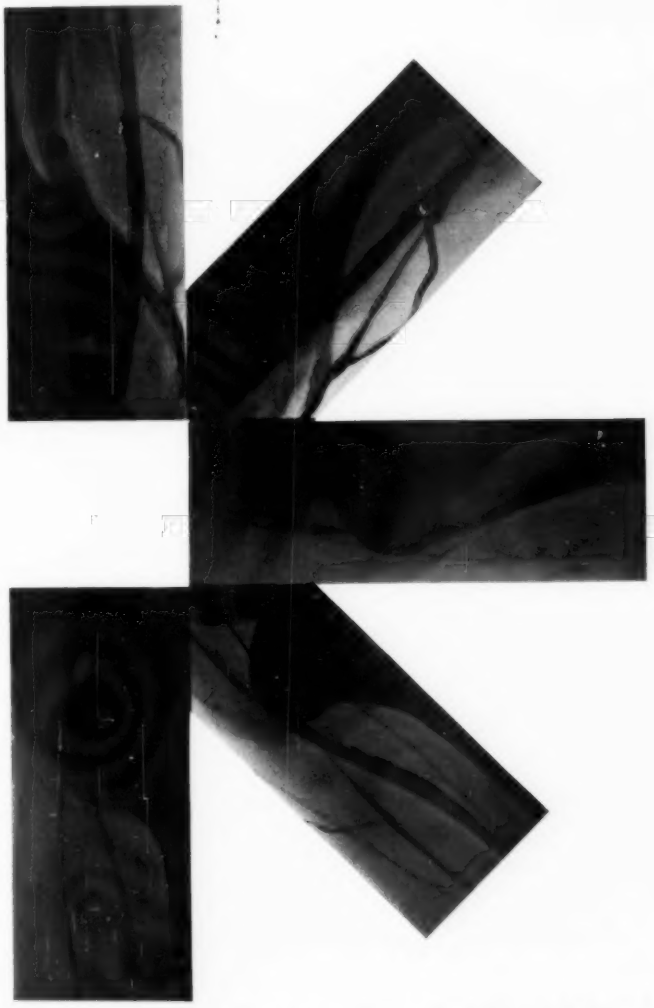


Fig. 6. The same extremity examined at different angles. The thickness of the layer of contrast medium in the popliteal and saphenous veins varies in spite of the amount of contrast medium (30 ml) and the injection time (30 sec.) being constant. No layer formation at angles of 90° or 45° in the erect position. With the limb horizontal the layer of medium in the distal (left) part of the popliteal vein is thin because the medium is flowing downwards. (Compare Fig. 7 a.) Note especially the incomplete filling of veins with the extremity elevated to 90°.

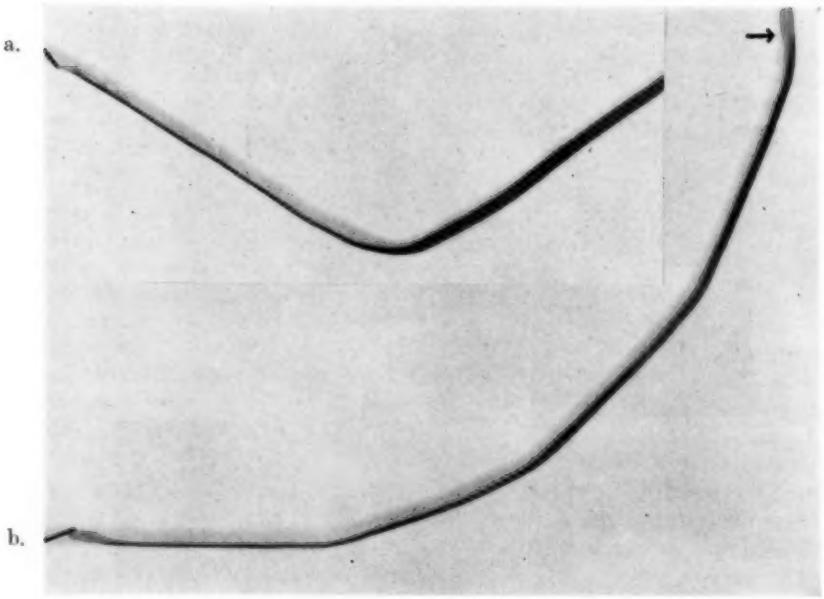


Fig. 7. The glass tube in Fig. 4 replaced by a flexible rubber tube. Direction of the flow from left to right.

a. Thin layer of contrast medium when flow is downwards, thick layer when upwards. Compare conditions with extremity horizontal, Fig. 6.

b. If the incline becomes successively greater the thickness of the layer of contrast increases. When the tube becomes vertical the contrast medium distributes itself over the whole lumen (→).

er has been able to verify this observation and has found experimentally that in this way contrast media will follow the superior wall of a tube for several inches, and that in an absolutely vertical tube, with the blood current directed upwards, a laminar flow, which will appear as a 'layer formation', may be obtained.

It is thus not possible to decide the degree of inclination of the extremity solely on the basis of experiments in vitro; experiments in vivo are necessary. With this in view, LÖFSTEDT has carried out comparative phlebographies on patients with insufficiency of the veins, in both the supine and sitting postures. In 1946, he reported on 16 cases; since then he has examined 14 more cases in the same way. The whole material was selected, in so far as only patients with large varices were included. In 7 of these 30 cases no contrast filling of the deep veins was obtainable,

irrespective of the technique used. In the remaining 23 cases the contrast filling was satisfactory in the sitting position and patency of the deep veins demonstrated. When a phlebographic examination was made of the same 23 cases with the leg in a horizontal position, 9 of the cases showed no contrast filling, and 3 cases only a partial filling, of the deep veins. Thus in this material the horizontal technique furnished an incorrect result in 40 % of cases. LÖFSTEDT's examinations must be regarded as a decisive argument for the use of a vertical position of the leg in phlebography.

During phlebography in the erect position, the patient may sometimes faint. If he is standing against a vertical table, he cannot topple backwards if syncope should occur, but a fall is possible in any other direction. (HÖJENSGÅRD has described a case of concussion in connection with phlebography.) If, on the other hand, the table is given such an angle that the patient can recline backwards (Fig. 12 b) the situation can be mastered in quite a different way, should syncope occur. The table may then be lowered to the horizontal plane. The work is thus carried out with a far greater feeling of confidence. The author has found that a 65° angle of the table is suitable, the patient then being in a comfortable position. In 10 cases this tilt of the extremity has been compared by means of d. exams. with phlebography of the absolutely vertical extremity. Only in one case could an improvement in the quality of the phlebogram be noticed when the angle was increased from 65° to 90°. In this patient the pathologic femoral vein was better filled at 90°. In another case the contrast filling of the iliac vein was decidedly better at 65° than at 90°. *Phlebography of an extremity at an angle of 65° to the horizontal plane can therefore be considered as equivalent to phlebography of a vertical extremity from a practical point of view.* (Hereafter a slope of 65° is inferred when speaking of phlebography on a patient in the erect position, or of phlebography on a vertical extremity.)

As the examinations made by LÖFSTEDT have exclusively been carried out on patients with very large varices and a somewhat different technique used, the author has in 27 cases made comparative phlebographies from an unselected material in both the erect and supine positions.

When the vertical technique has been used, 60 ml of Umbradil 35 % has been injected in every case, while with the horizontal technique the same amount has only been used in 11 cases. It has been found in 10 d. exams. that the contrast medium in an extremity horizontally placed flows away so quickly, that no improvement of the phlebogram is produced if the amount of contrast medium is increased from 20 to 60 ml (Fig. 8). In 16 cases, only 20 ml of contrast medium has therefore been used in the dorsal position. The rapid flow of contrast medium in an extremity horizontally placed also means that there is not time enough to examine the pelvis. Only the leg and thigh are therefore included in the comparative examination.

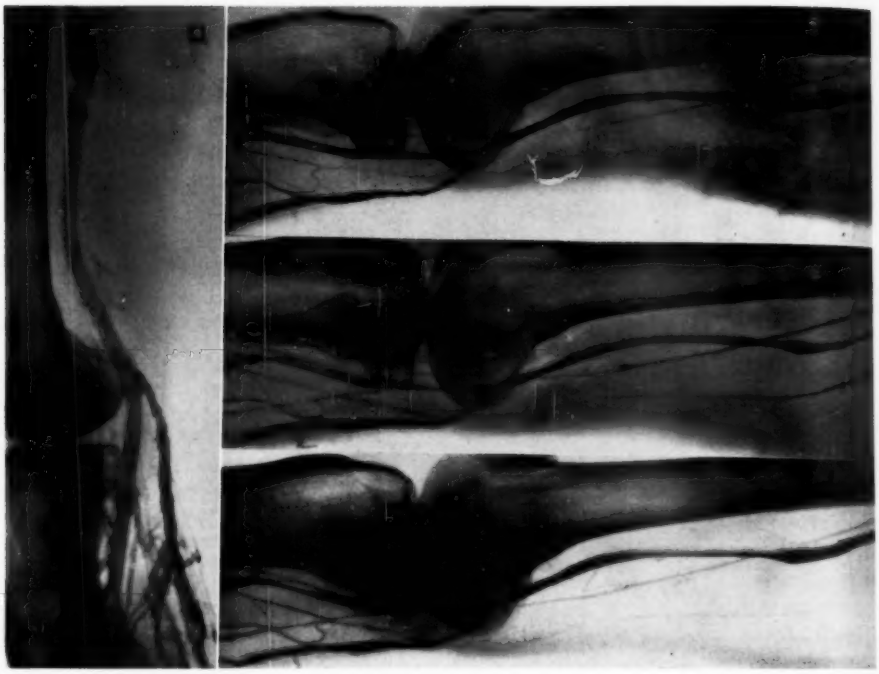


Fig. 8. Same extremity examined. a. Leg vertical, 60 ml Umbradil 35 % injected. b. Leg horizontal 20 ml Umbradil 35 % injected. Note the incomplete filling. c. 60 ml Umbradil 35 %, leg horizontal. Same findings as in b, thus there is no improvement in the filling in the horizontal position in spite of the increased amount of medium. d. 20 ml Umbradil 35 % with Macrodex. Limb horizontal. Same findings.

In this material also there is a great discrepancy between the findings on 'vertical' phlebography and those obtained on 'horizontal' phlebography (Figs. 9, 10). In all the 27 cases the vertical examination showed patency of the deep veins, while with the horizontal technique only partial filling of the deep veins was demonstrated in all cases and a continuous filling of the deep veins was absent in not less than 12 cases. If the question is: "Is there a free passage into the deep veins or not?" an affirmative answer based on the horizontal technique will be incorrect in more than two-fifths of the cases, as noted in this material.

BAUER (1946, 1951) has contended that the great dilatation of the veins that arises if the leg is placed in a vertical position is a decided drawback and, amongst other things, increases the difficulty of interpretation. For this reason he recommends the use of phlebography with the leg

placed horizontally. A dilatation of the veins is, however, no disadvantage if the exposure technique is adjusted to the degree of density of the object. In phlebography it is never difficult to so expose the film (high kV, low mAs) that all vascular details become clear.

It is quite a common observation, that the *superficial* veins of the forearm and lower part of the leg become dilated if the position of the extremity is changed from the horizontal to the vertical plane. The question of the dilatation of the *deep* veins is probably somewhat more complicated. BAUER's knowledge is founded on observations, made during operation. In 1951 he wrote: "In a large number of cases we have had the opportunity of seeing with our own eyes the exposed popliteal vein increase in volume two to four times if the foot-end of the operation table is lowered to an angle of 45°." BAUER considers this to be a normal physiologic condition which will occur even when the vein is not exposed. This conclusion is, however, not justifiable. When a vein is laid free, the pressure from the surrounding tissue is relieved and the vein can expand in quite a different way than under normal conditions. In fact, it may be verified roentgenologically whether the deep veins change in volume or not in different positions.

a. b.

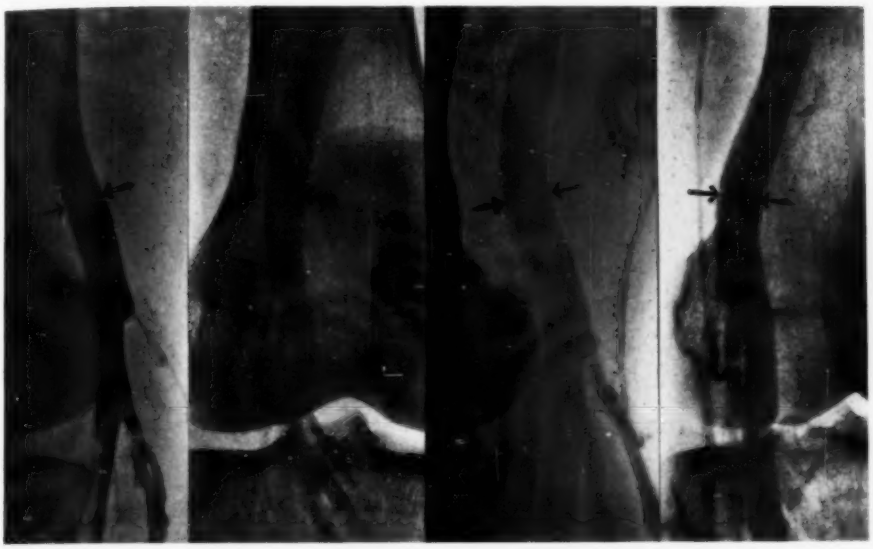
Fig. 9. a. Phlebogram in the horizontal position. Note the incomplete filling of the deep veins. b. Same extremity examined in the vertical position.

The comparative phlebographies which have been performed, both on horizontal and vertical extremities, provide the necessary material for measurements in vivo. As the deep veins of the lower leg may be difficult to identify, especially when incompletely filled in the horizontal phlebograms, measurements have been made only of the popliteal vein. When the examinations have been carried out with the leg vertical this vein has been completely filled. In the cases examined horizontally, those in which the vein has been at least half filled with contrast medium, were

a. b. c.

Fig. 10. a. Horizontal position. Incomplete filling of the deep veins.
b, c. Vertical extremity. Deep varices in the thigh.

used for comparative measurements (Fig. 11). It is obvious that when taking measurements in horizontal phlebograms it is necessary to be extremely careful and critical and only 15 out of 27 d. exams. have been found suitable. It has been possible to study layer formation as the films have always been taken with the roentgen beam directed horizontally. The horizontal phlebograms are obtained with the extremity free from support except at the heel, and consequently no deformity of the vein due to pressure need be taken into account. As the injection is made over 20 to 60 sec., an interval of about 5 sec. between the exposures with horizontally and vertically directed rays cannot be of any importance (two unsynchronized tubes with a short exposure time of 0.04 to 0.06 sec. were used). The result of these examinations was as follows: Out of 15 extremities with venous insufficiency the greatest difference in the



a. b. c. d.

Fig. 11. Estimation of the width of the popliteal vein in a horizontal extremity (a, b), and a vertical extremity (c, d). Scale 1 : 2. In the vertical position the popliteal vein is completely filled (the contours are well defined). When the leg is horizontal, more than half the lumen of the popliteal vein is filled at 7 cm above the knee-joint (a. compared with c.). The diameter in the frontal view is 12 mm (b) and the corresponding diameter in the vertical extremity, 13 mm. There is thus a dilatation of 1 mm.

diameter of the popliteal vein measured was 2 mm (10 mm in a horizontal extremity and 12 mm in a vertical one). In 4 cases there was no difference at all and in 6 cases the difference was only 1 mm. Furthermore 5 cases without any noticeable venous insufficiency were measured and the greatest difference in the width of the popliteal vein was found to be 1 mm (9 mm in the vertical leg, and 8 mm in the horizontal). If from these figures the volume is calculated (as mentioned by BAUER), or better the area, as it is a cross-section we are discussing, we obtain instead of a fourfold variation, a variation of at the most about 50 %. The "enormous dilatation of the veins caused by contrast medium" that BAUER talks about, must thus be considerably reduced in its proportions. As has already been mentioned, the dilatation as such does not interfere with the roentgenologic interpretation.

The deep veins vary only very slightly in width in different positions even in cases with considerable venous insufficiency. This does not mean that they may not be pathologically dilated. In 26 extremities

without any signs of venous insufficiency (17 females and 9 males, average age 23 years) examined by phlebography in the vertical position, the largest popliteal vein measured was 13 mm in diameter. Thus in no case did the popliteal vein attain anything approaching the size of that shown in Fig. 3 where the maximal diameter reaches 30 mm.

Contrast medium. A water-soluble contrast medium of the Umbradil, Diodrast, diodone etc. type is nowadays almost exclusively used for vascular examinations. In arteriography a comparatively highly viscous liquid — dextran (= Macrodex) — has been added to a water-soluble contrast medium of low viscosity (BACKMAN 1951) in order to improve filling, especially in the smaller vessels. From a theoretical point of view such an added ingredient is a disadvantage in phlebography. KJELLBERG pointed out in 1943 that low, rather than high, viscosity fluids mix best with another fluid of high viscosity, such as blood. In phlebography the difficulties are first of all due to the disinclination of the contrast medium to mix with the blood, and a contrast medium of low viscosity should therefore be used. The author has been able to verify KJELLBERG's statement, in experiments on mixing carried out *in vitro*. He has also found the same tendency to layer formation prevailing both with and without the addition of Macrodex in phlebography on an extremity horizontally placed (Fig. 8). In an examination made with the author's technique, there was no improvement in the result when Macrodex was added (1 d. exam.). Ordinary Umbradil is of low viscosity, slightly greater than that of water, and is therefore well suited for phlebography. Initially the author used it in a 50 % concentration in about 60 phlebographies. However, since 2 cases of thrombophlebitis of the superficial veins occurred in pelvic phlebographies performed in the supine position, the 50 % contrast medium has been abandoned. It was also found that better filling of the thigh and pelvic veins was obtained by using 60 ml Umbradil 35 % in about 200 cases than was obtained with 40 ml Umbradil 50 % in another series of 60 patients. This observation which was further verified by 3 d. exams. using equivalent amounts of contrast medium (40 ml 50 % = 57 ml 35 %) gave rise to the idea of first injecting the contrast medium in a 50 % solution and then in decreasing concentration. (In 10 d. exams., the results after injections of 69 ml contrast medium 35 % have been compared with the results after injections of 20 ml 50 % + 30 ml 35 % + 20 ml 17½ %.) No improvement in the results was obtained in this way, the only difference being that the contrast obtained became fainter in the lower part of the leg. Nor does a 25 % solution (10 d. exams. with 80 ml 25 %, and 57 ml 35 %) offer any advantage over a 35 %, which is exclusively used.

Most authors consider 20 ml of contrast medium to be a suitable amount to use for phlebography. As has already been pointed out, no

improvement is gained in the contrast filling of a leg horizontally placed if the quantity of the contrast agent injected is increased. But is this the case if phlebography is carried out on a vertical leg? The results after injections of 20 ml and of 60 ml Umbradil 35 % have been compared in 6 d. exams. In only one of these 6 cases was any contrast filling obtained in the upper part of the femoral vein and the iliac vein when using 20 ml of contrast medium in the erect position, while with 60 ml, good filling was obtained in all 6 cases. It is thus clear that 20 ml is insufficient and that an increase in the amount of contrast medium will improve the result if the examination is carried out on a vertical leg. An injection of 40 ml of contrast medium resulted in filling of the iliac vein in 3 out of 6 cases, while there was good filling in all the cases right up into the pelvis when 60 ml was used. Thus 40 ml of contrast medium was sufficient in half of these cases. When the dose was increased from 60 to 80 ml, only a very slight improvement in the filling of the pelvic veins was obtained in 2 out of 10 cases. In 4 cases in which the iliac vein was not filled by an injection of 60 ml, there was also no filling when using 80 ml. On pelvic phlebography in these 4 patients, the iliac veins were shown to be patent. It is, therefore, of very little advantage to inject 80 ml as a routine measure; 60 ml is enough in most cases and if no contrast filling of the pelvic veins is obtained with this quantity the examination should be supplemented by pelvic phlebography.

To summarize the results it may be said that in the case of a patient standing erect, 60 ml of ordinary Umbradil (diodone, Diodrast) should generally be used. In the case of an extremity of small volume and with minor varices, 40 ml of contrast medium 35 % may exceptionally be found satisfactory.

Injection technique. Many authors (LÖFSTEDT, HÖJENSGÅRD, et al.) have already pointed out that the method of exposing a vein, as recommended by DOS SANTOS, BAUER and HOMANS is not only unsuitable, due to the risk of ulceration developing in the devitalized tissues, but is also unnecessary. It is always possible to perform percutaneous injection, at least in all cases suffering from chronic venous insufficiency. If the puncture is carried out with precision, which is essential if a good result is to be gained, all risk of making a perivenous injection is eliminated. The swelling around the vessel that SULAMAA has noticed time and again, is the result of a bad puncture. It is advisable to use OLOVSON's heparin needle; this may be left in the vessel and a further injection made if necessary. It is now generally agreed that the puncture should be carried out as distally as possible, preferably on the dorsum of the foot. The material from Södersjukhuset which consists of more than 800 phlebographies, was examined after we had punctured veins both medially and laterally on the dorsum of the foot without our finding that the result

was in any way dependent upon which had been selected for injection. The author has, in order to obtain further verification in this matter, carried out a few d. exams. In 2 of the cases the injection was made medially at the base of the great toe, and also laterally on the dorsum of the foot, the findings being identically the same in both instances. In 3 cases, including 1 d. exam., the injection was made at the level of the malleoli and gave satisfactory results. Following injection in the middle of the lower leg (2 d. exams.) retrograde filling of the 3 double veins down to the ankle was obtained in one case. But in the other case the contrast filling of the deep veins was unsatisfactory in the distal third of the lower part of the leg. Thus to make sure of obtaining satisfactory contrast filling of the deep veins of the lower leg, the injection should preferably be made distal to the ankle. The injection may be made anywhere on the dorsum of the foot, although the lateral side or a medial vein at the base of the great toe is preferable. The veins in a medio-proximal position on the dorsum of the foot are not so well fixed in the subcutis, and therefore more difficult to puncture.

The importance of the injection time has also been studied. In 10 cases the injections have been: 1) rapid (60 ml in 1 min.), and 2) very slow (60 ml in 3 min.). In 6 cases in which the flow of the contrast fluid was rapid, exceptionally bad contrast filling was obtained with the longer period of injection, and a very satisfactory filling with the rapid injection. In the remaining cases only a very slight or no improvement was obtained with the rapid injection. In all of these cases the circulation was slow, and contrast filling of the thigh was only obtained towards the end of the examination. Fast injection is thus of essential importance in cases with rapid circulation. The puncture should therefore be made with a relatively wide bore needle (0.9 to 1 mm needle of 0.5 to 0.6 mm internal diameter), which is always possible, and the puncture must be precise, this being imperative for obtaining a good result.

In order to decrease the filling of the superficial veins and impel the contrast to follow the deep veins, the use of a tourniquet has been recommended around the malleoli (Bauer, Mahorner, Leriche and Servelle, Löfstedt, Moore, et al.) or around the knee (Adameck and Friedländer, Moore, Höjensgård, et al.) or an elastic bandage around the lower part of the leg (Bauer, Löfstedt). The elastic bandage should be evenly wound and not drawn too tight, as otherwise the risk of completely compressing both the superficial and deep veins arises; this will create a section with empty veins within the limits of the maximal compression (Fig. 12). Ten cases have been examined both with and without a tourniquet around the ankles. In 4 cases the findings were identical whether a tourniquet was used or not. In 6 cases there was a decrease in the filling of the superficial veins when a tourniquet was used,

while the contrast filling of the deep veins only improved in 2 of these 6 cases, and in 1 case it even decreased. The differences observed were not of any diagnostic importance in any of the cases. HÖJENSGÅRD has used a tourniquet at the level of the knee as a routine method and describes a case in which the deep veins were well filled when a rubber tube was used in this manner, but were not filled at all without a tourniquet. The author has examined 10 patients, with and without a tourniquet around the knee, but in no case found such a difference. The sole advantage of a tourniquet so applied is that fewer of the superficial veins become filled. This was the case in 7 out of 10 cases.

Five d. exams. have been made with and without an elastic bandage. Fewer of the superficial veins were filled in 4 out of these 5 cases when a bandage was used, but only in 2 cases did it bring about a slight improvement in the filling of the deep veins. Five more cases have been examined with both an elastic bandage and a tourniquet around the malleoli, and also without either one or the other. In all 5 cases the filling of the superficial veins was less when the compression methods were used. At the same time a better filling of the deep veins was obtained in 2 cases, and a less satisfactory filling in 1 case. There is therefore not much to be gained by the use of compression methods, the gain usually being restricted to a decreased filling of the superficial veins, which to some extent makes it easier to judge the deep veins. These methods may therefore be reserved for cases with large varices. If the exposure technique is correct, and the films obtained in two planes, there is as a rule

a. b.

Fig. 12. a. Compression too great. A region void of vessels has arisen proximally in the lower leg. b. Same extremity without any elastic bandage.

no difficulty in identifying the deep veins, even if the superficial ones are filled.

Both LINDBLOM and LÖFSTEDT claim that muscular movements assist the flow of the contrast medium. In 10 d. exams. the author has been able to confirm that the contrast filling proximally in the thigh and the pelvis improved considerably in 8 cases when the patient was made to carry out muscular movements (with the front part of the foot remaining in position, the patient lifts the heel and bends the knee, the heel then being lowered again and the knee extended). The improvement in these cases is so marked that it cannot have been due to chance. In the 2 remaining cases the improvement was only slight. As it is difficult to obtain good filling of the pelvic veins it is advisable to start the muscular movements immediately before exposure of the films of the pelvis; this, however, should not be done until the two first films are taken because if the flow is rapid, the lower leg, and possibly also the thigh, may be emptied of contrast medium.

LINDBOM recommends massage of the superficial veins. Following massage (10 d. exams.) improvement of contrast filling proximally was prominent in 1 case, slight in 3 cases, and absent in 6 cases. These findings allow no definite conclusions to be drawn, but it seems probable that the routine use of massage is of little importance.

Conclusions

As long as we are restricted to the use of contrast fluids which form layers with blood, phlebography must be carried out on an extremity vertically placed and with the blood-flow ascending. If a percutaneous injection is made, the puncture must be precise. In order to examine the veins of the lower extremities a comparatively large amount of contrast medium is usually necessary (60 ml Umbradil 35 %, diodone or similar agents). The extremity in a vertical position, a puncture of precision and a sufficient amount of the contrast medium are the three factors of decisive importance. Rapid injection and energetic muscular movements often improve the result to a certain extent.

A summary of the technique developed by the author is appended.

The technique is a modification of the one presented by LÖFSTEDT (1946). In agreement with LÖFSTEDT the author considers it necessary that the films should be taken in two planes at right angles. By examining the patients in the erect, instead of the sitting position, films of the pelvis may also be obtained as a routine measure (Fig. 13). LINDBLOM in 1941, HÖJENSGÅRD in 1949, SYLWAN in 1950 and SCOTT and ROACH in 1951 have performed phlebographies on patients standing, without taking advantage of this possibility. The author has striven to find a technique through which the deep veins of the whole of the extremity as well as those of the pelvis may be studied. (In all cases in which no contrast filling of the external iliac vein is obtained, special phlebo-

a. b. c.

Fig. 13. Films of the pelvis, taken in routine phlebography using the technique described. a. Normal case. b. Patient with venous insufficiency. Varices in clumps high up in the thigh and pubic region; the iliac vein is patent. c. Patient with clinical signs of acute thrombosis. Only the upper part of the femoral vein (→) is filled in a retrograde direction. Contrast medium flows through the thigh via the profunda femoris, the concomitant femoral and the great saphenous veins (from left to right); the iliac vein is patent.

graphy of the pelvis should be carried out.) Phlebography of the pelvis will be discussed in a later article.

The patient stands reclining against the examination table, placed at 65° to the horizontal plane. In cases with varices an elastic bandage is applied to the lower leg. A clean puncture is made into a vein on the dorsum of the foot, OLOVSON's heparin needle being suitable for this purpose. The needle should be fixed with strapping and 60 ml Umbradil 35 % (diodone, Diodrast) rapidly injected in about one minute. The first film is exposed immediately after the end of the injection and the rest of the films are then taken as rapidly as possible. (The author obtains 10 films in about 3 minutes.) The work is carried out with two tubes, one for the frontal and one for the lateral view. Films in two planes are obtained both of the lower part of the leg and of the thigh. When using

60 ml of contrast medium, one frontal and one lateral view of the lower leg are sufficient. Only films with sagittally directed rays are taken of the pelvis, as the contrast filling is usually too poor to show the veins in a lateral projection; the exposures of these (4) films are spread over the whole examination. Immediately before the exposure of the last films of the pelvis the patient should perform energetic muscular movements. For the frontal views of the thigh as well as for those of the pelvis, a secondary diaphragm, preferably a Lysholm grid, is used. The films should be well exposed (high kV and low mAs). In order to facilitate the handling of the cassettes the author has designed a simple cassette-holder.

More than 400 phlebographies have been carried out with this technique in our Department. No serious complications have arisen. In a few cases (less than 5) superficial thrombophlebitis has occurred in the vein on the dorsum of the foot, where the injection has been made. No thrombosis of the deep veins has been observed at any time. The secondary ill-effects following the injection of water-soluble contrast media containing iodine have occurred with about the same frequency as in intravenous urography.

SUMMARY

A technique for ascending phlebography on an extremity vertically placed is described. The technique is based on experimental and practical investigations.

ZUSAMMENFASSUNG

Eine Technik für die ascendierende Phlebographie bei vertical gelagerter Extremität wird beschrieben. Die Technik gründet sich auf experimentelle und praktische Untersuchungen.

RÉSUMÉ

Description d'une technique de phlébographie ascendante sur un membre placé verticalement. Cette technique est fondée sur des recherches expérimentales et pratiques.

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FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROFESSOR KNUT LINDBLOM), KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN

THE CORRELATION BETWEEN CONTRAST EXCRETION AND ARTERIAL AND INTRAPELVIC PRESSURES IN UROGRAPHY

An experimental study in rabbits

by

N. P. G. Edling, C. G. Helander and *L. Renck*

In 1932, v. LICHTENBERG described the nephrographic effect in urography with the help of which the situation, shape and size of the kidneys are more clearly visualized than in conventional radiography. Further observations on this subject were made by HELLMER (1942) who demonstrated the possibilities of a structural analysis of the kidney in nephrograms in urinary stasis. WICKBOM (1950) studied the influence of the blood pressure in urography and described two cases in which there was no contrast filling of the renal pelves when the blood pressure fell to about 70 mm Hg. He reported agreement with the general experience in renal physiology that urinary excretion ceases when the systolic blood pressure falls to this level. WICKBOM's two cases showed a simultaneous increase in the density of the kidney shadows; this finding was, however, not discussed in detail. EDLING (1952, 1953) presented cases illustrating the nephrographic effect during shock in urography. He presumed that when the filtration pressure of the glomeruli decreases with the fall in blood pressure, the contrast medium excreted by the functioning tubular epithelium cannot flow into the pelves. LINDGREN (1953) produced an intentional lowering of the systolic blood pressure to about 90 mm Hg in order to increase the intensity and duration of the nephrographic effect during aortography under general anaesthesia.

For a more detailed study of the correlation between contrast excretion and arterial and intrapelvic pressures in urography the present

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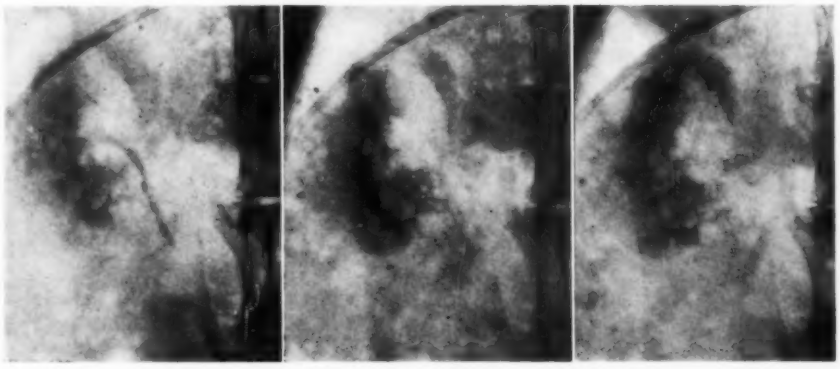
authors have performed investigations experimentally in rabbits. The intention has also been to see whether the findings agree with those described to date in human subjects. The investigations included urography during variations in the blood pressure and intrapelvic pressure.

Methods

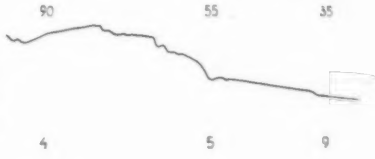
The rabbits were anaesthetized with ether, firstly with an open mask and then through a catheter inserted into the trachea by means of an incision. After dissecting the carotid artery on one side, a cannula was introduced and connected to an instrument for kymographic registration of the blood pressure. Heparin was injected into the cannula to prevent coagulation and 5 to 8 ml of Umbradil 35 or 50 % were given via an aural vein, that is 1 to 2 ml/kg body weight.

The *blood pressure* was lowered by various methods so that contrast filling of the pelves ceased but the circulation in the kidneys remained intact. Three animals were given inhalations of amyl nitrite. In three cases a ganglion-blocking agent was injected intravenously, two of these having received azamethonium bromide, and one hexamethonium iodide. In one animal the fall in blood pressure was caused by intentional overdosage of the ether, and in another by bleeding after one femoral vein had been



a. b. c.

Fig. 1. (Only the right kidney reproduced.) a. 18 min. after injection of 6 ml Umbradil 35 %. Blood pressure 90 mm Hg. No nephrographic effect. Contrast filling of pelves and ureters. b. 27 min. Blood pressure 55 mm Hg. Slight nephrographic effect. No contrast filling of pelves and ureters; these have emptied. c. 42 min. Blood pressure 35 mm Hg. Nephrographic effect as in b. No contrast filling of pelves and ureters.



Blood pressure curve. Hypotensive agent, azamethonium bromide (1 + 0.5 + 5 mg). The upper figures indicate the pressure in the carotid artery when the films in a, b and c are exposed, the lower the serial numbers of the films.

Fig. 2. 22 min. after injection of 5 ml Umbradil 35 %. 5 mg azamethonium bromide. Slight blood pressure fall to 95 mm Hg. Head tilted downwards. No nephrographic effect. Contrast filling of pelves and ureters which are distended.

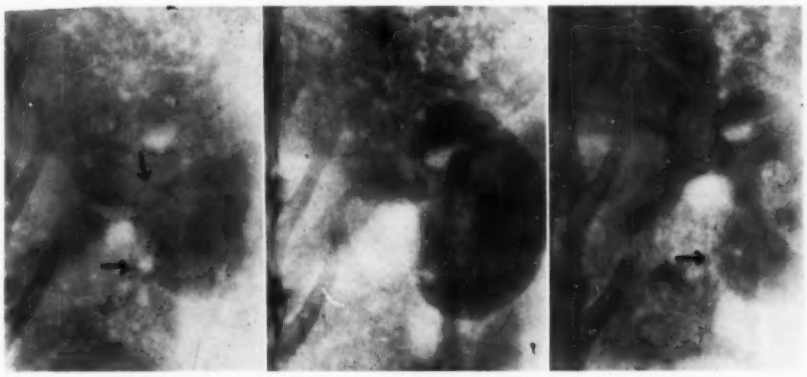
dissected and a cannula introduced. During the course of the examinations the blood pressure was continually registered, and exposures were made successively at two or three minute intervals.

When the *intrapelvic pressure* was varied the blood pressure was maintained at a sufficiently high level to prevent a nephrographic effect due to blood pressure fall. In order not to injure the renal pelvis, the distal part of the left ureter was dissected as close to the bladder as possible and a polyethylene catheter (1 mm) introduced in a cranial direction. When free passage of urine commenced through the catheter the contrast medium was injected intravenously. After the contrast excretion into the pelves had started, the distal part of the catheter was elevated vertically to allow the urine level to rise until there was a hydrostatic balance between the glomerular filtration pressure and the intrapelvic pressure. The height of the fluid in the catheter was measured in mm and no further counterpressure was used. As previously the blood pressure was registered and exposures were made. Three animals were examined, two of them twice.

For comparison another four healthy rabbits were examined under ether anaesthesia, one without and one with compression and two after application of the blood pressure registration apparatus. No other interventions were done.

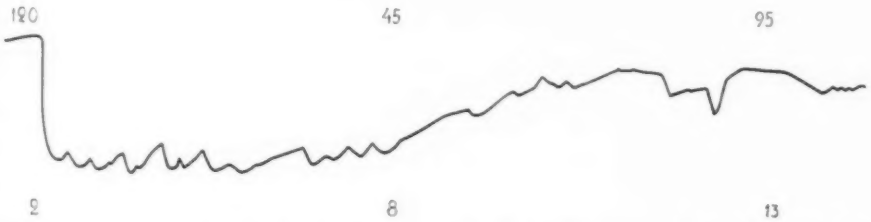
Results

During the examinations of the rabbits there was no or only a transient variation in the blood pressure due to the injection of the contrast medium, in spite of the fact that the doses of Umbradil were large compared with the blood volume of the animals. Without pressure variations the contrast excretion soon started with partial contrast filling



a. b. c.

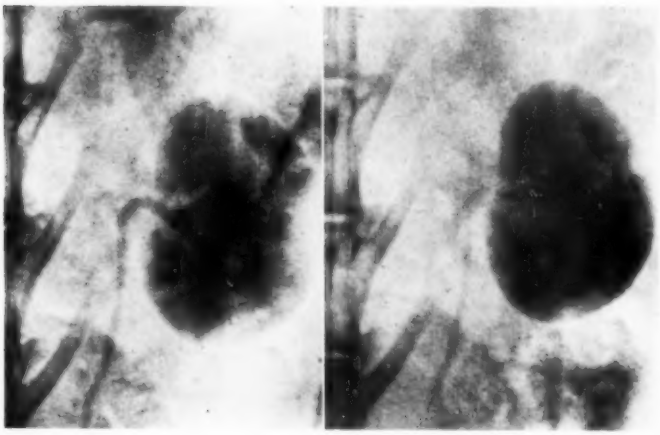
Fig. 3. (Only the left kidney reproduced.) a. 5 min. after injection of 8 ml Umbradil 50 %. Blood pressure 120 mm Hg. No nephrographic effect. Contrast filling of pelves and ureters. b. 18 min. Blood pressure 45 mm Hg. Nephrographic effect. No contrast filling of pelves or ureters. c. 32 min. Blood pressure 95 mm Hg. The nephrographic effect has decreased considerably. Contrast filling of the ureters.



Blood pressure curve. Hypotensive agent, amyl nitrite. The upper figures indicate the pressure in the carotid artery when the films in a, b and c are exposed, the lower the serial numbers of the films.

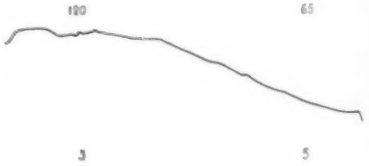
of the pelves and ureters, no definite nephrogram being obtained (Figs. 1 a, 6 a, b, c right side). When the operating table was lowered into the Trendelenburg position, stasis and dilatation of the pelves and proximal parts of the ureters were demonstrable but no nephrographic effect was observed (Fig. 2). In the case with compression of the ureters, stasis, but again no nephrographic effect, occurred.

When the *blood pressure* was lowered by means of amyl nitrite, azamethonium bromide or hexamethonium iodide, the findings in all cases were essentially the same. The contrast excretion started in a normal way when the Umbradil was injected before the above prepara-



a. b.

Fig. 4. (Only the left kidney reproduced.) a. 6 min. after injection of 8 ml Umbradil 50 % by means of a venous cannula. Blood pressure 120 mm Hg. Nephrographic effect and contrast filling of pelves and ureters. b. 16 min. Blood pressure 65 mm Hg. Intensified nephrographic effect. The pelves and the right ureter have emptied; left ureter still partly contrast filled due to compression by the distended bladder.

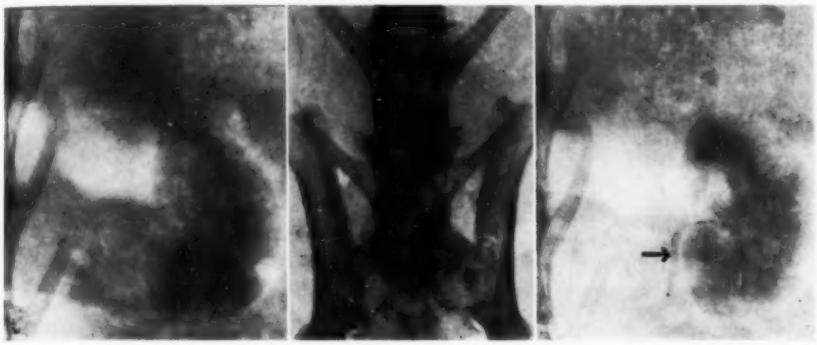


Blood pressure curve. Blood pressure fall as a result of bleeding. The upper figures indicate the pressure in the carotid artery when the films in a and b are exposed, the lower figures the serial numbers of the films.

tions were given (Fig. 1 a). After the inhalation or intravenous injection of the hypotensive agent, the blood pressure fell more or less abruptly (curves Figs. 1, 3, 5). This was followed by accumulation of the contrast medium in the kidneys instead of a filling of the pelves which continued to empty (Figs. 1 b, c, 3 b, cp. 4 b). When the blood pressure rose again, usually spontaneously, to 60 to 70 mm Hg contrast filling of the pelves again appeared (Figs. 3 c, 5 c) and the nephrographic effect decreased (Fig. 3 c).

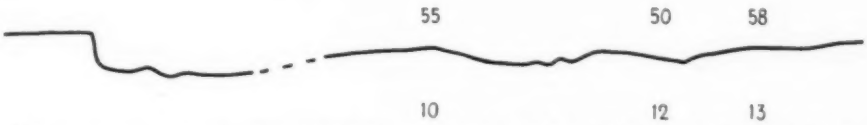
With a fall in blood pressure to 30 to 35 mm Hg, there was no contrast filling of the pelves and only a slight nephrographic effect (Figs. 1 c, 5 a and curve Fig. 5), until the blood pressure rose to about 60 mm Hg (Fig. 5 c). The last findings indicate that at a very low blood pressure the function of the kidneys is impaired.

The animal that was anaesthetized by an overdosage of ether showed



a. b. c.

Fig. 5. (Only the left kidney reproduced.) a. 41 min. after injection of 8 ml Umbradil 50 %. Blood pressure 55 mm Hg. Slight nephrographic effect. No contrast filling of pelves or ureters. b. 48 min. Blood pressure 55 mm Hg. No contrast filling of the bladder. c. 51 min. Blood pressure 58 mm Hg. Moderate nephrographic effect; partial contrast filling of the pelves and ureters.

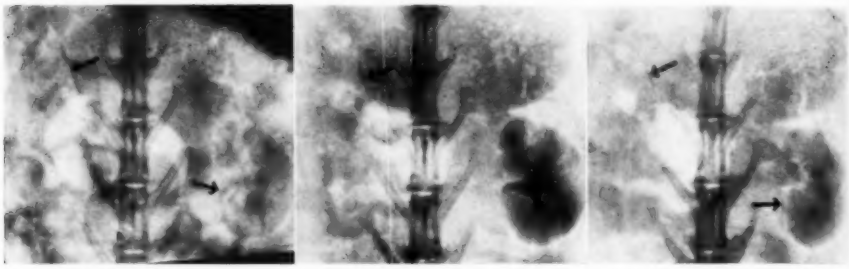


Blood pressure curve. Hypotensive agent, amyl nitrite. The upper figures indicate the pressure in the carotid artery when the films in a, b and c are exposed, the lower the serial numbers of the films. Blood pressure in the beginning only 60 mm Hg.

a slow fall in blood pressure from 90 to 40 mm Hg just before death. At between 70 to 60 mm Hg, both kidneys increased in density and the contrast filling of the pelves ceased, being in agreement with the other cases in which the blood pressure was lowered.

When the blood pressure fall was caused by bleeding, it decreased gradually from 120 to 35 mm Hg just before death. In this case the contrast medium was rapidly injected by means of the cannula introduced into the femoral vein. After two minutes a moderate nephrographic effect and contrast filling of the pelves could be demonstrated simultaneously due to the very high concentration of Umbradil (Fig. 4 a). With further decreases in blood pressure the nephrographic effect became more marked and, at 65 mm Hg, the contrast filling of the pelves was inhibited, while the emptying still continued (Fig. 4 b).

The *intrapelvic pressure* was increased by means of the hydrostatic pressure in the raised ureteric catheter. The fluid levels rose to different



a. b. c.

Fig. 6. Catheter in the left ureter. a. 8 min. after injection of 8 ml Umbradil 50 %. Blood pressure 90 mm Hg. Left side: Counterpressure in the catheter starts. Increasing nephrographic effect and partial contrast filling of the pelves and uppermost part of the ureter. Right side: No nephrographic effect. Contrast filling of the ureter. b. 32 min. Blood pressure 120 mm Hg. Left side: Counterpressure 700 mm fluid. Enlarged kidney. Marked nephrographic effect. Contrast filling and distension of pelvis and uppermost part of ureter. Right side as in a. (Contrast filling of bladder.) c. 59 min. Blood pressure 80 mm Hg. Left side: No counterpressure. Kidney size and nephrographic effect decreased. The pelvis has emptied and the catheter is contrast filled. Right side and bladder as in a.

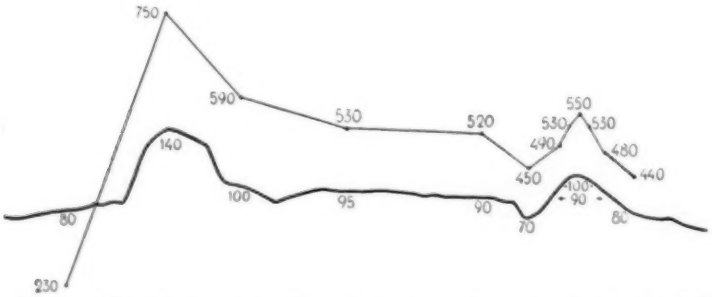


Fig. 7. Curves of blood pressure and counterpressure in a catheter in the left ureter. The upper figures indicate the counterpressure in mm fluid, the lower the pressure in the carotid artery in mm Hg. The figures demonstrate the correlation between the arterial pressure (glomerular filtration pressure) and the intrapelvic pressure.

heights in the various examinations, the greatest being 750 mm. Stasis with dilatation of the pelvis and a marked nephrographic effect appeared in all cases (Fig. 6 a and b). When the catheter was lowered so that urine could flow out, the pelvis emptied with contrast filling of the catheter and the nephrographic effect decreased (Fig. 6 c). On three occasions corresponding variations in the blood pressure and the hydrostatic pressure in the catheter could be demonstrated (cp. Fig. 7).

Discussion

The different methods of decreasing the blood pressure produce the same results in the excretion of contrast medium by the kidneys during urography. At a pressure of 60 to 70 mm Hg the contrast filling of the pelves ceases and the density of the kidneys increases due to accumulation of the medium. The arterial pressure in the glomeruli is about two-thirds of the systolic pressure and, at the level just named approximately as great as the sum of the colloidal osmotic pressure of the plasma and the intratubular pressure. An alteration in the intrapelvic pressure in one kidney by means of counter pressure in the ureter, with consequent reduction in the filtration pressure of the glomeruli, produces the same impairment of the excretion of the contrast medium. When the blood pressure rises or the intrapelvic counter pressure is removed, accumulation of contrast medium decreases and during the rise in blood pressure the contrast filling of the pelves again appears. These findings indicate that the nephrographic effect in urography is caused by variations in the intraglomerular or intrapelvic pressures — as occurs in human subjects in shock or stasis.

It is naturally of great interest to know where the contrast medium accumulates during the nephrographic effect. In view of the intravenous injections this cannot be in the capillaries as seen in the early phase of renal arteriograms. In historadiographic investigations of the situation of Diodrast in the rabbit kidney in urography ENGSTRÖM and JOSEPHSON (1953) have observed the iodine in the tubular cells and lumina after the injection of massive doses of the substance (8 ml Diodrast 35 %/kg body weight). When small doses were given none of the medium could be demonstrated in histologic sections, although chemical determinations indicated the presence of a considerable concentration of iodine in the renal tissue. The urographies of ENGSTRÖM and JOSEPHSON were performed without intentional impairment of the renal function. In our series there is undoubtedly a much higher concentration of iodine in the kidney when the accumulation is macroscopically visible as the nephrographic effect. The accumulation is most marked when the glomerular filtration pressure is reduced to about 0, indicating that the nephrographic effect depends in the main on the function of the tubular cells and to a lesser extent on the filtration through the glomeruli. We therefore consider it reasonable to presume that the uptake of the contrast medium into the tubular epithelium is unimpaired but the flow of urine into the pelvis impossible due to the reduction in the filtration pressure. Further studies of the situation of the contrast medium are however necessary.

When the contrast excretion into the pelves has ceased, the pelves

have emptied, indicating a neuromuscular function independent of variations in the filtration pressure.

As stated above, the blood pressure must not be lowered too much or the examination performed in a moribund animal. When the renal circulation fails the tubular cells cannot function and no nephrographic effect appears. This also occurs in human subjects in severe shock.

SUMMARY

The investigation carried out in rabbits indicates that the nephrographic effect in urography depends upon variations in the arterial and intrapelvic pressures. With a lowering in the systolic blood pressure the contrast medium accumulates in the kidneys and the filling of the pelves ceases as occurs in shock in human subjects. When the intrapelvic pressure is increased there is again an accumulation of contrast medium comparable to that found in stasis in man.

ZUSAMMENFASSUNG

Die an Kaninchen durchgeführte Untersuchung zeigt, dass der nephrographische Effekt bei der Urographie auf Schwankungen des arteriellen und intrapelvischen Druckes beruht. Bei Senkung des systolischen Blutdruckes speichert sich das Kontrastmittel in den Nieren und die Füllung des Nierenbeckens hört auf, wie es beim menschlichen Schock der Fall ist. Wenn der intrapelvische Druck zunimmt, geschieht wieder eine Anhäufung des Kontrastmittels, die mit der bei der Stauung beim Menschen gefundenen vergleichbar ist.

RÉSUMÉ

Ces recherches effectuées sur des lapins montrent que l'effet néphrographique dans l'urographie dépend de variations de la pression artérielle et de la pression dans le bassinet. Quand la pression systolique sanguine s'abaisse, le produit de contraste s'accumule dans les reins et le remplissage des bassinets cesse, comme cela se produit au cours du choc chez l'homme. Quand la pression dans les bassinets augmente, il y a encore une accumulation du produit de contraste, comparable à celle que l'on trouve dans la stase chez l'homme.

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THE PNEUMOGRAPHIC ASPECT OF THE ANGIORETICULOMA (HEMANGIOBLASTOMA) OF THE CEREBELLUM

by

Giovanni Ruggiero and *Francesco Castellano*

A tumour in the posterior fossa in a patient over 30 years of age and with no suggestion of metastases is probably either an acoustic neurinoma, a meningioma or an angioreticuloma. The roentgenologic signs of an acoustic neurinoma are characteristic and well known (LYSHOLM, LINDGREN, REVILLA, LUNDBORG). Using the material of Serafimerlasarettet the authors have carried out a fairly complete study on meningiomas of the posterior fossa, with particular regard to the roentgenologic aspects. The ventriculographies of several cases of cerebellar angioreticuloma were also re-examined in an attempt to establish certain differential criteria in meningiomas of the posterior part of the posterior fossa, *i. e.* between those attached to the tentorium and to the dura of the cerebellar convexity. The purpose of the present paper is to define the radiologic aspects of the cerebellar angioreticuloma by a detailed study of these cases.

Literature

As far as we are aware, the only systematic study on the roentgenologic features of the cerebellar angioreticuloma is the one carried out by DYKE and DAVIDOFF in 1942. The results of their work were reported later by DAVIDOFF and EPSTEIN. In a series of 24 cerebellar cases (GARDNER and NOSIK, 1942) in which lumbar encephalography was inadvertently carried out, there were four angioreticulomas. PERLMUTTER, HORRAX and POPPEN (1950) reported the end-results of 25 verified cases of cerebellar angioreticuloma; air studies were necessary for the diagnosis in 17 cases. In 1938 LYSHOLM, in his exhaustive study of the ventriculographic picture

Submitted for publication, Nov. 1, 1953.

of brain tumours, established the principles of the generic diagnosis of the cerebellar tumour. In his series there were ten cases of cerebellar angioreticuloma.

Other cases of cerebellar angioreticuloma with roentgen documentation are scattered throughout the literature. In many of these, however, the radiologic diagnosis was not the primary consideration and, moreover, the technique of the roentgen examinations was insufficient. For these reasons, we consider a more detailed review of the literature unnecessary.

Case Summaries

(angrt. = angioreticuloma; op. = operation)

The material of this study consists of 15 cases of cerebellar angioreticuloma observed from 1942 at the Roentgen Department and the Neurosurgical Clinic of Serafimerlasarettet, Stockholm.

1. ♀ 24. Op. (NORLÉN): angrt. in the left cerebellar hemisphere. Headache for 6 months. One attack of unconsciousness. Progressive diminution of vision. Involvement of the right 5th nerve. Cerebellar signs on the left. Romberg and nystagmus present. Bilateral choked disks 2 diopters. Rtg.: negative. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked; fourth ventricle dilated and displaced 1.5 cm to the right with a bulge in the left wall.

2. ♂ 33. Op. (NORLÉN): angrt. in the left cerebellar hemisphere. Headache for 3 months. Unstable gait. Bilateral choked disks 1—2 diopters. Slight bilateral cerebellar signs. Positive Romberg. Rtg.: negative. Encephalography (suboccipital puncture): no filling of the ventricular system. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked; fourth ventricle dilated and displaced to the right.

3. ♂ 49. Op. (NORLÉN): angrt. in the left cerebellar hemisphere. Headache for 18 months. Poor vision. Diplopia. Unstable gait. Bilateral choked disks: R = 4; L = 5 diopters. Cerebellar signs on the left. Romberg and nystagmus present. Rtg.: negative. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked; fourth ventricle dilated and displaced to the right.

4. ♂ 25. Op. (NORLÉN): angrt. in the fourth ventricle and right cerebellar hemisphere. Vertigo for 5 months. Headache and progressive diminution of hearing on the right side. Bilateral choked disks 3 diopters. Romberg and nystagmus present. Rtg.: calvarium more vascularized than normal. Ventriculography: hydrocephalus; marked upward displacement of the posterior part of the third ventricle; aqueduct dilated and slightly displaced to the left; fourth ventricle almost entirely filled by a mass from the right (Figs. 1 and 2).

5. ♂ 51. Op. (FRYKHOLM): angrt. in the right cerebellar hemisphere. Headache for 14 months. Poor equilibrium. Diplopia. Progressive diminution of hearing probably bilateral. Bilateral choked disks 2—3 diopters. Positive Romberg. Right facial palsy. Rtg.: decalcification of the posterior part of the floor and of the dorsum of the sella turcica. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked; fourth ventricle dilated and displaced to the left.

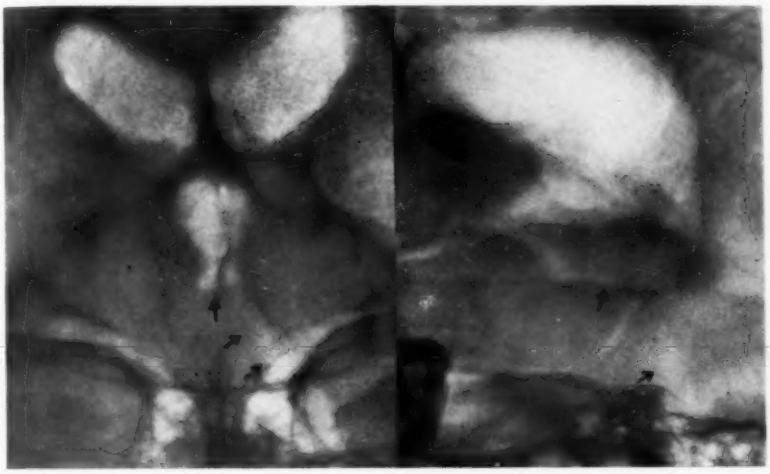

Fig. 1. Fig. 2.

Figs. 1 and 2. Case 4. Ventriculography. Aqueduct dilated and, together with fourth ventricle, pushed upwards, slightly backwards, and markedly to the left. The fourth ventricle is almost entirely occupied by the tumour. Best visualization of the filling defect in the fourth ventricle was obtained in the oblique film with the right side up (Fig. 2).

6. ♂ 47. Op. (OLIVECRONA): angrt. in the right cerebellar hemisphere. Headache for 12 months. Vertigo and poor vision. Bilateral choked disks 4 diopters. Right cerebellar signs. Rtg.: negative. Ventriculography: hydrocephalus; posterior part of the third ventricle displaced upwards; aqueduct displaced forwards and kinked; fourth ventricle dilated and displaced to the left with a bulge from the right.

7. ♀ 33. Op. (NORLÉN): angrt. in the right cerebellar hemisphere. Headache and vertigo for 2 months. Weakness. Sleepiness. One generalized epileptic seizure. General condition poor. Bilateral choked disks 3 diopters. Peripheral right facial palsy. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards, kinked and displaced to the left together with fourth ventricle.

8. ♀ 50. Op. (OLIVECRONA): angrt. in the left cerebellar hemisphere. Headache for 12 months. Poor equilibrium. Choked left disk 2—3 diopters. Optic atrophy on the right. Almost blind in right eye. Nystagmus. Involvement of the fifth nerve on the left. Rtg.: very large bregmatic veins. Encephalography (suboccipital puncture): the air entered a cavity which very probably was the tumoral cyst.

9. ♂ 39. Op. (OLIVECRONA): angrt. in the left cerebellar hemisphere. Mental tiredness and instability of temper for 12 months. Headache. Poor equilibrium. Bilateral choked disks 2—3 diopters. Left cerebellar signs. Positive Romberg and nystagmus. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked about 0.5 cm from its origin from the third ventricle; fourth ventricle displaced to the right.

10. ♂ 34. Op. (OLIVECRONA): angrt. in the left cerebellar hemisphere. Headache for 12 months. Poor equilibrium and diminution of vision. Markedly choked disks: R = 9; L = 7 diopters. Poor general condition. Blind. Positive Romberg. Involvement of the fifth nerve bilaterally and seventh on the right side. Rtg.: negative. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked; fourth ventricle poorly filled and displaced to the right.

11. ♂ 29. Op. (OLIVECRONA): angrt. in the right cerebellar hemisphere. Headache for 24 months. Vertigo. Poor equilibrium. Bilateral choked disks 3 diopters. Positive Romberg and nystagmus. Rtg.: marked convolutional impressions; posterior part of the floor and dorsum of the sella turcica poorly calcified. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards, kinked about 0.5 cm from its origin from the third ventricle; fourth ventricle dilated and displaced to the left.

12. ♂ 55. Op. (OLIVECRONA): angrt. in the right cerebellar hemisphere. Headache for 36 months. Poor equilibrium. Bilateral choked disks 4—5 diopters. Left cerebellar signs. Romberg and nystagmus present. Rtg.: dorsum sellae poorly calcified. Ventriculography: hydrocephalus; upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked; fourth ventricle dilated and displaced to the left.

13. ♂ 54. Op. (OLIVECRONA): angrt. in the left cerebellar hemisphere. Headache for 4 months. Vertigo. Bilateral choked disks: R = 2; L = 3 diopters. Bilateral cerebellar signs, more marked on the right. Positive Romberg. Bilateral involvement of fifth nerve. Rtg.: negative. Encephalography (suboccipital puncture): no air entered the ventricular system. Ventriculography: markedly asymmetric hydrocephalus the left ventricle being much wider than the right; septum pellucidum and third ventricle displaced towards the left side; marked upward displacement of the posterior part of the third ventricle; aqueduct displaced forwards and kinked about 1 cm from its origin from the third ventricle; fourth ventricle displaced to the right.

14. ♀ 25. Op. (OLIVECRONA): angrt. in the left cerebellar hemisphere. Headache for 8 months. Progressive diminution of vision. Diplopia. Bilateral choked disks: R = 4; L = 5 diopters. Cerebellar signs on the right side. Romberg and nystagmus present. Rtg.: decalcification of dorsum sellae; destruction of the posterior part of the floor of the sella turcica. Ventriculography: hydrocephalus; septum pellucidum slightly displaced to the left; posterior part of the third ventricle displaced upwards; aqueduct dilated, displaced forwards and kinked; fourth ventricle dilated and displaced about 1 cm to the right with a bulge in its left wall (Figs. 3, 4 and 5).

15. ♀ 24. Op. (NORLÉN): angrt. in the right cerebellar hemisphere. Headache with transient diplopia, diminution of vision and impairment of equilibrium for four years. Vomiting for three weeks. Nuchal rigidity. Bilateral choked disks: R = 1; L = 2 diopters. Rtg.: negative. Ventriculography: hydrocephalus; posterior part of the third ventricle displaced upwards; aqueduct displaced forwards and to the left; fourth ventricle displaced forwards and to the right with marked bulging from the right.

Discussion

Conventional Radiograms. Ordinary roentgen examination of the skull was performed in 12 cases and was negative in 5. Signs of increased vascularization of the skull without signs of intracranial hypertension were present in 2 cases (Nos. 4 and 8). Such a finding — though of no localizing

Fig. 3.

Fig. 4.

Fig. 5.

Figs. 3, 4 and 5. Case 14. Characteristic ventriculographic film of cerebellar angioreticuloma. Aqueduct and fourth ventricle dilated and markedly displaced forwards and to the right. Aqueduct kinked. Bulge from the left into the fourth ventricle. Best demonstration of the filling defect in the fourth ventricle was obtained in the oblique view with the left side up (Fig. 4). In the oblique film with the right side up (Fig. 5) the fourth ventricle appears dilated but only slightly deformed.

value — should be taken into consideration when the presence of a cerebral tumour is ascertained by other means of investigation since it may be indicative of a highly vascularized lesion. Signs of increased intracranial pressure were observed in 4 cases, or 33 per cent; they were marked in only one (No. 14). In the series of DYKE and DAVIDOFF these signs were present in 8 out of 13 cases, and they were usually limited to a slight atrophy of the sellar region. The relatively high incidence of cases without routine roentgen examination in both series, may be responsible for fatal diagnostic errors. In fact, the clinical picture, especially at its onset, may consist chiefly of headache which, in some cases, may even be the only symptom. In these cases the absence of roentgenologic signs of

increased intracranial pressure may influence the examiner in ruling out the possibility of the presence of a brain tumour.

Ventriculography. Ventriculography was carried out in 14 cases and demonstrated a tumour in the posterior fossa. More or less marked hydrocephalus was always present. The lateral ventricles were asymmetric in all cases, and in all but one the left was wider than the right. In one case the asymmetry was so marked that the septum pellucidum was displaced towards the smaller ventricle. In the series of DYKE and DAVIDOFF, asymmetric dilatation of the lateral ventricles was observed in six cases. In one of these, one ventricle was almost 2 cm wider than the other as seen in the a.-p. view. In the same series there were also three cases in which the septum pellucidum was slightly deviated to one side. The authors do not say whether or not in these latter cases there was also asymmetry of the lateral ventricles. Such asymmetry was observed by us also in cases of meningioma. In our opinion, this should be considered as the result of an increase, due to the hydrocephalus, of the congenital difference between the lateral ventricles, with a prevalence of the left, as already emphasized by LINDGREN.

The posterior part of the third ventricle was displaced upwards in every case. This displacement is usually observed in all tumours of the posterior fossa, but it seems more marked in the intracerebral parenchymatous growths (RUGGIERO and CASTELLANO).

The aqueduct and fourth ventricle were contralaterally displaced in all cases, and pushed forwards in all but one. The fourth ventricle was also dilated in many of the cases. A comparison between the lateral and frontal views is indispensable for evaluating the dilatation of the fourth ventricle. In fact, if the fourth ventricle is compressed laterally by a tumour, its antero-posterior diameter becomes longer. The fourth ventricle may therefore appear dilated on the lateral view although only elongated. The aqueduct was visualized in 11 of the 13 cases of the series of DYKE and DAVIDOFF. It was dilated in 9. The fourth ventricle, on the other hand, was visualized in only four cases. Ventriculography was performed in 16 cases of the series of PERLMUTTER, IRWIN, HORRAX, GILBERT and POPPEN; the aqueduct and fourth ventricle were visible in only three cases. In our opinion, the discrepancy between, on the one hand, the data of the series of DYKE and DAVIDOFF and PERLMUTTER, HORRAX and POPPEN, and, on the other hand, those of the present series is imputable to the difference of techniques employed. A special manoeuvre for filling the aqueduct and fourth ventricle is performed as a routine measure in the roentgen examination of the posterior fossa, and it proved to be indispensable in a great number of cases. If the aqueduct and fourth ventricle are not visualized after this manoeuvre, it is practically certain that the non-

filling of these parts of the ventricular system is due to some anatomic obstruction and not to a technical error. In a series of 15 cases of tentorial meningioma, in which ventriculography had been performed according to the technique used in cases of cerebellar angioreticuloma, the writers of the present article found that the entire aqueduct and fourth ventricle were visualized in only four cases. This difference, in our opinion, is due to the site of the tumour and may also be caused by the nature of the lesion. A tentorial meningioma, by displacing the contents of the posterior fossa forwards and downwards, provokes (often at an early stage) a kinking of the aqueduct. The same condition occurs in intra-cerebellar tumours in the superior part of the vermis. In such cases, even with small tumours, the fourth ventricle becomes difficult or impossible to fill with air. The quadrigeminal plate is kinked, its lower part displaced forwards and compression occurs at its lower margin. The further the process lies from the middle line, the more marked will be the lateral displacement; at the same time, the forward displacement will be decreased and it appears that the conditions necessary for compression will be lessened. The importance of the site is confirmed by the fact that in meningiomas of the cerebellar convexity which have a posterior-inferior and lateral site of attachment, the fourth ventricle is usually well visualized as in tumours of the cerebellar hemispheres.

In Case 4, of a tumour growing partly in the fourth ventricle, the aqueduct was not kinked forwards but pushed backwards and upwards. A large filling defect was present in the fourth ventricle (Figs. 1 and 2). Deformity of the fourth ventricle was observed in four more cases (Nos. 1, 6, 14 (Figs. 3, 4, and 5) and 15). Oblique views and lateral views with a verticle beam projection are recommended for visualizing slight deformations of the walls of the fourth ventricle. In these positions the air collects in either side of the fourth ventricle (Figs. 2, 4 and 5). This finding is of great diagnostic value as it reveals the intracerebral nature of the lesion.

Encephalography. Encephalography by suboccipital injection carried out in the ward was performed in three cases of the present series. In two of these, no filling of the ventricular system was obtained and the examination was practically useless. In the other case the air entered directly into the tumoral cyst. In similar cases the exact diagnosis can be readily suspected. In our opinion, however, this method should be avoided. In fact, the suboccipital puncture may injure the cerebellar tonsils which are almost always herniated through the foramen magnum and often infiltrated by the tumour. Such an injury may cause severe bleeding.

One of us (R.) had the opportunity of performing lumbar encephalography according to LINDGREN's technique in a case of cystic cerebellar angioreticuloma at the Neurosurgical Clinic of Ste. Anne Hospital, Paris. In this case the aqueduct and fourth ventricle

were not visualized, but the diagnosis of a tumour in the left half of the posterior part of the posterior fossa was made on the basis of the changes in the basal cisterns: 1) flattening of the pontine cistern demonstrating the forward displacement of the brain stem; 2) upward displacement to the left of the vallecula cerebelli; 3) the filling defect in the inferior part of the great cistern, demonstrating cerebellar herniation which was later verified at operation (TALAIRACH).

Lumbar encephalography is generally regarded as a very dangerous procedure in cases of a tumour in the posterior fossa. On the other hand, GARDNER and NOSIK inadvertently performed lumbar encephalography in three cases of cerebellar angioreticuloma and no accident occurred. LINDGREN has described an encephalographic technique which permits the carrying out of lumbar encephalography even in cases of tumours of the posterior fossa with increased pressure, without greater risk than in ventriculography. In the case described the patient had markedly choked disks. Encephalography was performed by injecting about 10 ml of air by the lumbar route. The patient stood the examination very well although there was marked cerebellar herniation, and was successfully operated upon ten days later.

Differential Diagnosis. As it appears from the discussion on the ventriculographic material, the tentorial meningioma must be regarded as the most important possibility in the differential diagnosis. The essential points in the differential diagnosis may now be summarized.

1) In the angioreticuloma good filling of the fourth ventricle by ventriculography is obtainable. The fourth ventricle is very often dilated. Filling of the entire aqueduct and fourth ventricle, on the contrary, is only rarely obtainable in cases of tentorial meningioma.

2) A deformation of the fourth ventricle due to direct compression or invasion by the tumour is not rare in angioreticuloma. Such a finding was never observed in cases of meningioma and can, therefore, be regarded as almost pathognomonic of the presence of an angioreticuloma. (It is, of course, the only criterion for differentiating an angioreticuloma from a meningioma of the cerebellar convexity.)

3) In angioreticuloma, as practically in all intracerebral tumours of the posterior fossa, the upward displacement of the posterior part of the third ventricle is more marked than in meningioma.

4) Signs of direct involvement of the bone are present in some cases of meningioma.

SUMMARY

Fifteen case summaries of cerebellar angioreticuloma are presented. The routine examination of the skull showed signs of increased intracranial pressure in 33 per cent of cases. A forward and contralateral displacement of the aqueduct and fourth ventricle is a characteristic ventriculographic feature. The aqueduct is usually kinked and the fourth

ventricle dilated. Deformation of the fourth ventricles was present in one third of cases. Such a deformation is almost pathognomonic in adult patients. Lumbar encephalography may be useful in demonstrating the presence of cerebellar herniation. The problem of the differential diagnosis is discussed.

ZUSAMMENFASSUNG

Die Arbeit beschäftigt sich mit röntgenologischen Untersuchungen an 15 Fällen von Kleinhirn-Angioblastomen. Das einfache Röntgenbild des Schädels liess in 33 % der Fälle Zeichen intrakranieller Druckerhöhung erkennen. Das charakteristische Ventrikulographische Bild besteht in einer Verlagerung des 4. Ventrikels und des Aquaeduktes nach vorn und zu dem Tumor gegenüber liegende Seite. Hierdurch entsteht im allgemeinen ein scharfer Knick im Aquaedukt; der 4. Ventrikel ist oft erweitert. In 1/3 der Fälle war der 4. Ventrikel deformiert. Eine derartige Deformierung kann beim Erwachsenen als fast pathognomonisch angesehen werden. Die lumbale Encephalographie kann nützlich sein, da sie auch eine bestehende Einklemmung der Kleinhirntonsillen erkennen lässt. Die Differentialdiagnose der Fälle wird ausführlich besprochen.

RÉSUMÉ

Ce travail consiste en une étude radiologique de 15 cas d'angioréticulome (hémangioblastome) du cervelet. L'examen standard du crâne a montré des signes d'hypertension intracranienne dans 33 pour cent des cas. L'aspect ventriculographique caractéristique est un déplacement de l'aqueduc et du quatrième ventricule vers l'avant et vers le côté opposé à la tumeur. L'aqueduc est généralement coudé et le quatrième ventricule dilaté. Dans un tiers des cas le quatrième ventricule était déformé. Cette déformation doit être considérée comme presque pathognomonique chez un sujet adulte. L'encéphalographie par voie lombaire peut être utile en démontrant aussi l'engagement des amygdales cérébelleuses. Discussion du diagnostic différentiel.

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MALIGN TUMOUR OF THE SPLEEN DIAGNOSED BY LIENAL ARTERIOGRAPHY

by

Gunnar Edsman

Primary tumours of the spleen are rare. In 1945, BOSTICK gathered from the literature 157 cases of primary tumours of the spleen and then added seven of his own cases. He believed that all the tissues present in the spleen might be the cause of tumours and therefore divided the latter into seven different groups. Six of these types he found represented in the literature. Vascular tumours, *e. g.* lymphangiomata and haemangiomata, are the most common among BOSTICK's cases. Second come the lymphadenomata and third the group of tumours arising from the reticulo-endothelial cells, for instance, endothelioma and reticulum cell sarcomata. BOSTICK found eleven cases described in the literature of different kinds of cysts in the spleen.

In 1949, WRIGHT described a type of tumour in the spleen, which he called a haemangiosarcoma. This tumour has a tendency to produce metastases. He distinguished six tumours of this type among the cases described in the literature, and added one of his own. STORY and GIBBS, in 1952, mentioned a vascular pleumorphic sarcoma in the spleen with metastases in the liver, lungs, and skeleton. The same year LAFORET also described a primary sarcoma in the spleen.

It is difficult to diagnose a tumour of the spleen. The diagnosis was not secured in any of BOSTICK's seven cases at the clinical examination, but only at operation or autopsy.

Aortography has been performed in several cases of enlarged spleen at the Roentgen Department of Sahlgrenska Sjukhuset. A primary malign tumour of the spleen has been roentgenologically diagnosed by the free occurrence of pathologic vessels in an enlarged spleen. As a

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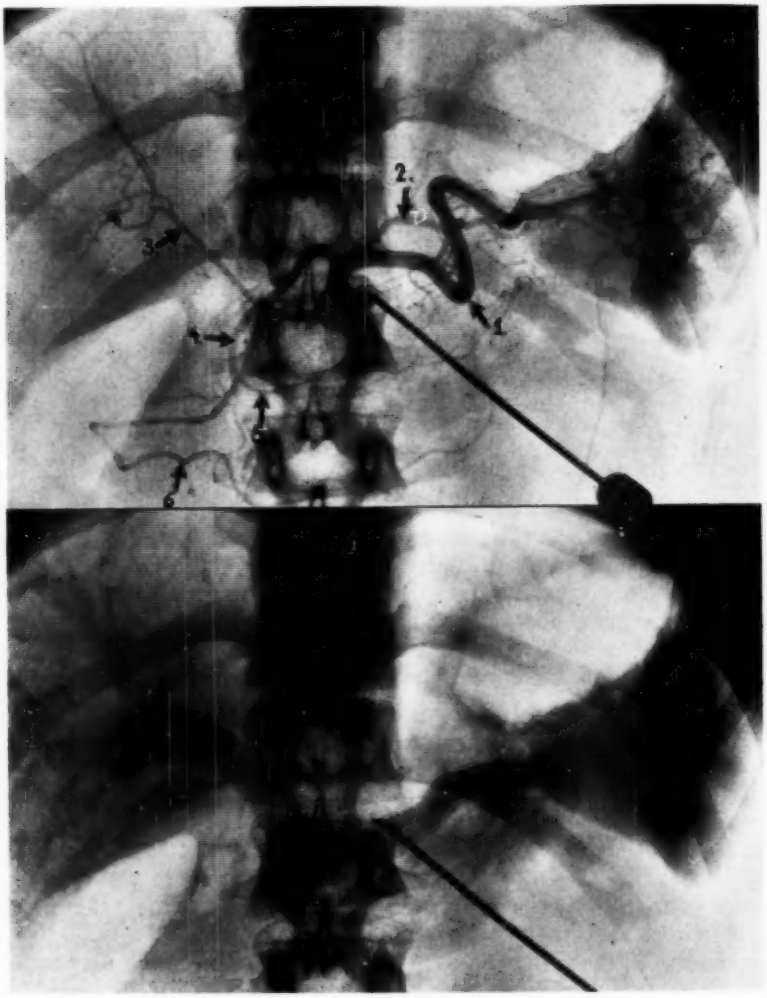
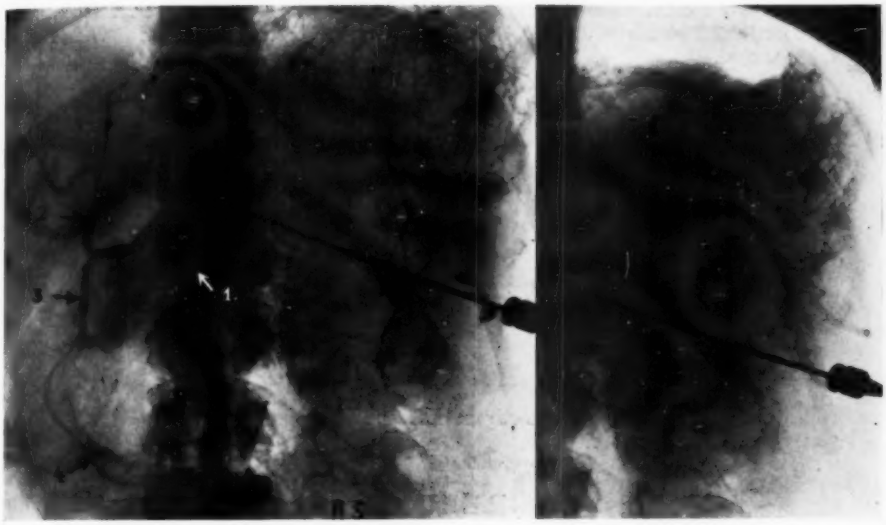


Fig. 1. Lienal arteriography. Normal case. a. 1. art. lienalis; 2. art. gastrica sinistra; 3. art. hepatica; 4. art. gastroduodenalis; 5. art. gastroepiploica dextra; 6. art. pancreaticoduodenalis sup. b. Same case 4 seconds later. Vena lienalis and vena portae contrast filled.

tumour of the spleen, as far as I am aware, has not been diagnosed previously by means of arteriography, the case is described below.



a. b.

Fig. 2. Lienal arteriography. Malign splenic endothelioma. a. 1. art. lienalis; 2. art. hepatica; 3. art. gastroduodenalis; 4. art. gastroepiploica dextra. Displaced left kidney. b. Two seconds later. Many pathologic vessels in the enlarged spleen.

No. 1110, female, born 1913. 1946: Pain in the abdomen and diarrhoea. 1947: Admitted to the Med. Dept; diagnosis: chronic colitis plus psychoneurosis. Continuous diffuse pain in the abdomen and nausea, until re-admission on 17 July 1951, to the Med. Dept. Splenomegaly present and on roentgen examination the length of the spleen was estimated at 19 cm. No enlargement of the liver. Roentgen examination of the stomach, colon and lungs normal. HB: 65 %. Red blood cells: 3.4 mill. White blood-corpuscles: 3,000. Index: 0.95. Differential count of the white blood-corpuscles was normal. Red blood cells without nucleoli in the peripheral blood. *Puncture of the spleen* on 2 August 1951, revealed no signs of tumour tissue or isolated tumour cells. No myeloid cells. Diagnosis: Splenomegaly plus colitis. Discharged: August 1951.

Re-admitted on 26 February 1952. During the interval continuous pain in the left of the abdomen. Resistance under the left costal margin with hard and somewhat dented mass to deep palpation. 3 March 1952: aortography (Figs. 2 a and b). The arteria lienalis was displaced medially, was tortuous, and divided at an early stage into coarse vessels, with markedly pathologic ramifications which ran to a considerably enlarged spleen. The arteria gastroduodenalis was coarse and the arteria gastro-epiploica dextra also sent pathologic vessels to the spleen. The stomach was displaced medially and the left kidney downwards.

17 March 1952: Operation (MOBERG). Spleen extirpation + colon resection with latero-lateral anastomose + pancreas resection + extirpation of metastasis in the liver. A large tumour, rich in vessels penetrating the entire spleen, was removed. Weight: 1,500 g. Pea-sized metastasis in the liver was extirpated. Histologic diagnosis: Malign

tumour of the spleen, probably endothelioma plus metastasis in the liver. The patient was re-examined in November 1953. No clinical signs of metastases. Blood values and weight normal.

At operation, the tumour of the spleen was in advanced stage. On clinical examination, eight months previously the spleen was found to be enlarged. The case indicates that lienal arteriography is justified in uncertain types of splenomegaly.

SUMMARY

A case of primary malign tumour of the spleen diagnosed by means of lienal arteriography is described.

ZUSAMMENFASSUNG

Ein Fall von primärem bösartigem Milztumor, diagnostiziert mit Hilfe lienaler Arteriographie, wird beschrieben.

RÉSUMÉ

Un cas de tumeur primaire maligne de la rate diagnosticée par une artériographie liénale est relatée.

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ON MICROTOMOGRAPHY

by

Knut Lindblom

The roentgen examination of living subjects is to-day still mainly a study of macroscopic anatomy. Two new fields of diagnostic roentgenology, the physiologic and histologic, however, appear to have come into

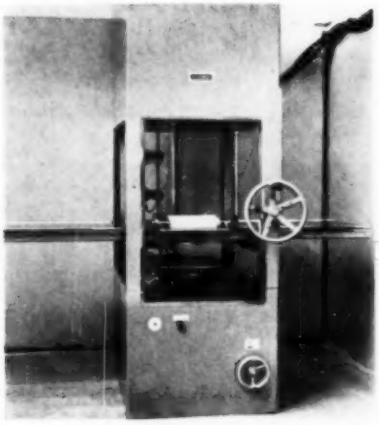


Fig. 1. Apparatus for tomography at small angles.

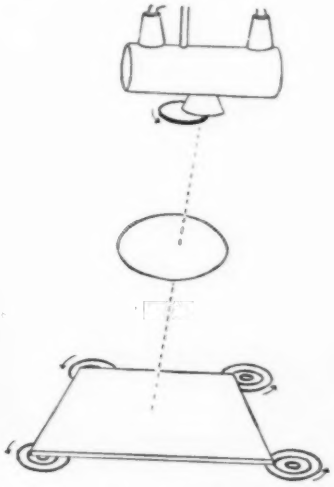


Fig. 2. The principles of the apparatus. Schematic.

existence. The former has been made possible by high voltage and image amplification, and the latter with the additional aid of micro-target tubes.

Paper read at the 7th International Congress of Radiology, Copenhagen, 1953; submitted for publication, June 23, 1954.

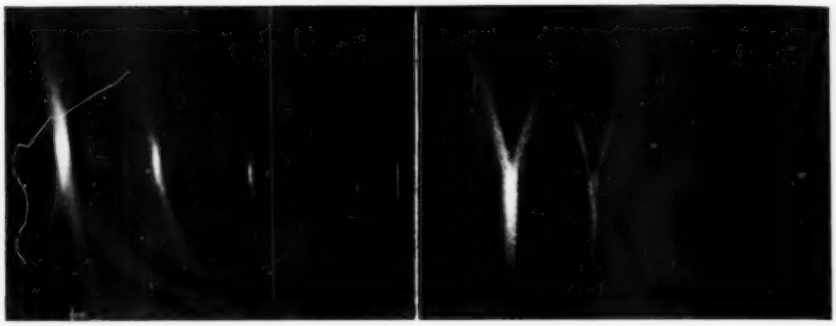


Fig. 3. Tomograms 1.0, 0.7, 0.4, and 0.2 mm metal threads placed almost perpendicular to the film. To the left the high definition of crossing centre with the apparatus described. To the right the moving centre with an apparatus for tomography at large angles.

By employing a target of 0.3 mm we have already been able to reach a direct magnification of twice the original image. By means of a target of 0.1 mm the direct magnification should be 5 times the original. High voltage should give adequate penetration and the image amplifier be of considerable assistance.

With the fluorescent material of the intensifying screens in immediate contact with the silver of the film, it should be possible to increase the

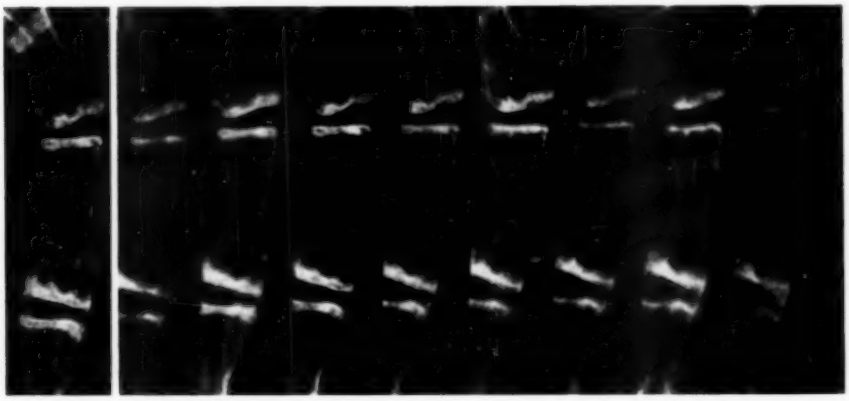
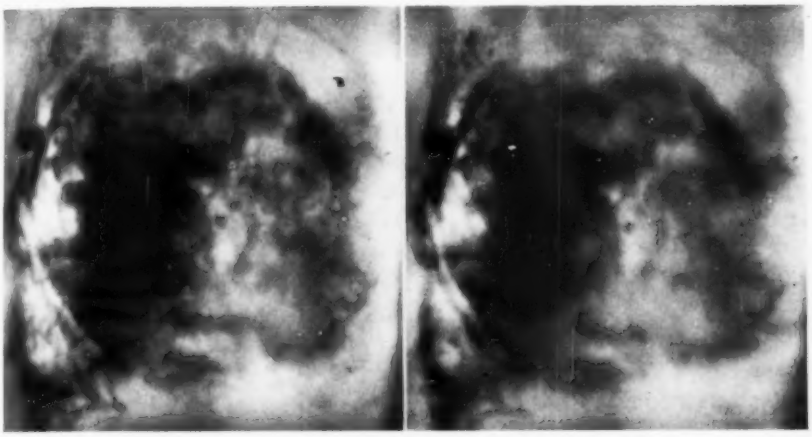


Fig. 4. Plain roentgenogram and tomograms of a rat's tail taken with the apparatus described. Direct magnification × 2. Distance between sections 1 mm. Note the difference in appearance of spongeous structures in the different sections as well as the absence of false circular structures.



a. b.

Fig. 5 a and b. Conventional roentgenogram (a) and tomogram (b) of specimen of tubal pregnancy taken with direct magnification × 5. Target 0.1 mm 200 kV. Water filter 10 cm. Note the selective appearance of small vessels and a venous sinus in the tomogram.

definition of the roentgenograms sufficiently to be enlarged × 2. The total magnification would then be 10 times, permitting visualization of the alveoli of the lung and, in angiography, the capillaries.

Without tomography there will be too many interfering structures in the microscopic films. The conventional apparatus for tomography cannot, however, be used for our purpose because of the lack of definition obtained. There are two reasons for this: the long exposure time and the distortion of the structures both caused by the relatively great angles of movement.

By using rotation tomography at small angles it is possible to overcome these drawbacks. The advantages were studied on a simple model and subsequently an apparatus for clinical use was built (AB Elema-Järnh, Stockholm). The exposure time for the examination of the chest is 0.05 to 0.1 sec. and the angle of movement 6° and 9° for magnifications of 3/2 and 2/1 respectively. At these angles the distortion of the structures is negligible.

The apparatus and its principles are illustrated in Figs. 1 and 2. The tube above the table rotates round a vertical axis at 4 cm from the target. The casette below the table makes synchronous movements on circular tracks, the diameter of which depends on the magnification desired.

The circular movement is supposed to cause false circular structures and the small angle is expected to increase the thickness of the defined

layers. As illustrated in Fig. 4 neither is true in tomography of structures of the body. Experiments only with metal phantoms are misleading.

The commercial tubes for clinical use have targets no smaller than 0.3 mm. In order to demonstrate the value of a still smaller target, an anatomic specimen with contrast-filled vessels was roentgenographed at 200 kV through a 0.1 mm pin-hole in a piece of lead. An ordinary roentgenogram as well as tomograms were taken, in both cases with a direct magnification $\times$ 5. The result is illustrated in Fig. 5. The specimen was a tubal pregnancy in which arteries of 0.1 mm of diameter as well as venous sinuses were visualized. The tomogram in Fig. 5 b shows such a venous sinus selectively.

SUMMARY

Microtomography of living subjects by means of a new apparatus is described. The further development of the method is discussed.

ZUSAMMENFASSUNG

Die Mikrotomographie lebender Patienten mit Hilfe einer neuen Apparatur wird beschrieben. Die weitere Entwicklung der Methodik wird diskutiert.

RÉSUMÉ

L'auteur décrit la microtomographie de sujets vivants au moyen d'un nouvel appareil. Il étudie les possibilités d'avenir de cette méthode.

AUS DEM RADIOPHYSIKALISCHEN INSTITUT (VORSTAND: PROF. R. SIEVERT), DER »KONUNG GUSTAV V:S JUBILEUMSKLINIK«, STOCKHOLM, SCHWEDEN

UNTERSUCHUNGEN ÜBER DIE STRAHLENSCHUTZ-VERHÄLTNISSE AN VERSCHIEDENEN UNIVERSALGERÄTEN

von

Erkki Himanka und *Lars Lorentzon*

Werte für die Strahlendosen, mit denen der Untersucher bei der Untertischdurchleuchtung bestrahlt wird, sind schon früher veröffentlicht worden (BENNER; BRAESTRUP; JACOBSON, SCHWARTZMAN und HEISER, u. a.). Mit dieser Arbeit beabsichtigen die Verfasser die Strahlengefährdung des Durchleuchters bei der Untersuchung liegender Patienten an zwei verschiedenen Typen von Arbeitsplätzen, nämlich Trochoskopen schwedischen Typs mit bis zum Fussboden reichenden Schutzschild und umlegbaren Universalgeräten zu vergleichen.

Abb. 1 zeigt das Prinzip der Untertischdurchleuchtung und die Placierung des Untersuchers. Die Füsse des Durchleuchters (A) werden von Sekundärstrahlung, die von dem Patienten, der Tischplatte und

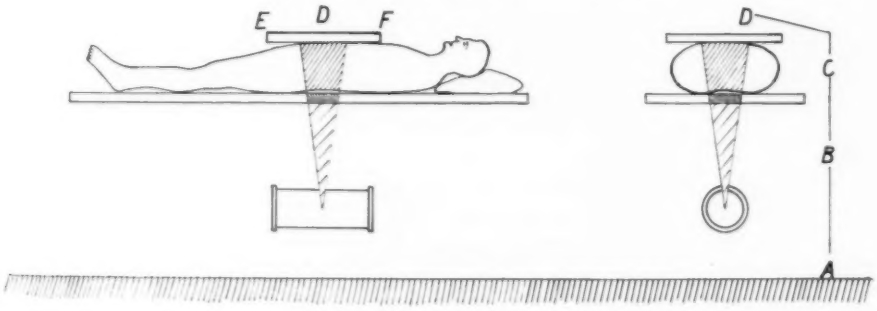


Abb. 1.

Bei der Red. am 26. Mai 1954 eingegangen.

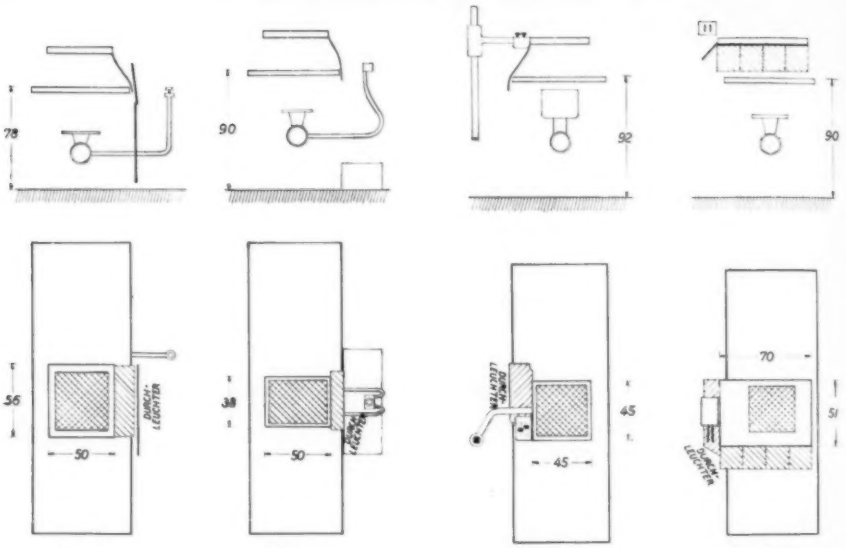


Abb. 2. Abb. 3. Abb. 4. Abb. 5.

Abb. 2. Trochoskopgerät schwedischen Typs.
Abb. 3. Umlegbares schwedisches Universalgerät.
Abb. 4. Umlegbares ausländisches Universalgerät.
Abb. 5. Umlegbares ausländisches Universalgerät.

der Luft kommt, getroffen. Die Knie (B) und der Körper (C) werden ausserdem von Sekundärstrahlung, die von den Blenden, dem Filter und ev. dem Röhrenfenster und dem Öl in der Haube herrührt, bestrahlt. Die von dem Patienten kommende Sekundärstrahlung muss, um den Körper des Durchleuchters bei C zu treffen, einen Teil des Patienten passieren und wird hierbei geschwächt (5—10 cm Gewebe absorbiert ungefähr ebenso stark wie 0.1 mm Blei). Je kleiner die Blendenöffnung gewählt wird, desto länger wird der Weg, den die Strahlung im Patienten passieren muss, um den Durchleuchter zu treffen. Der Kopf des Durchleuchters (D) kann nicht von Sekundärstrahlung getroffen werden. Die Nutzstrahlung wird nahezu völlig von der hinter dem Leuchtschirm befintlichen Bleiglasscheibe absorbiert. Die Unterarme des Durchleuchters (E und F) können im allgemeinen nur von solcher Strahlung getroffen werden, die schon durch den Körper des Patienten geschwächt worden ist.

Die zur Untertischdurchleuchtung verwendeten Geräte sind mit Strahlenschutzanordnungen verschiedener Art versehen. Um festzustellen, wie gross die Dosis ist, die der Durchleuchter bei der Untertischdurch-

Tabelle I

	Trochoskop schwedischen Typs (Abb. 2)	Umlegbare Universalgeräte		
		älteres schwedisches Gerät (Abb. 3)	ausländisches Gerät (Abb. 4)	ausländisches Gerät (Abb. 5)
Strahlenschutzanordnungen:				
Grösse des Leuchtschirmes mit Rahmen				
Breite	56 cm	38 cm	45 cm	51 cm
Tiefe	50 cm	50 cm	45 cm	70 cm
Am Leuchtschirm befestigter Bleigummilappen				
Breite	55 cm	45 cm	45 cm	50 cm | 70 cm
Länge	33 cm	35 cm	40 cm	16 cm | 20 cm
Schutzschild vor dem Durchleuchter				
Breite	70 cm	nicht	nicht	nicht
Höhe vom Boden	5—95 cm	vorhanden	vorhanden	vorhanden
Röhre-Leuchtschirm	frei beweglich	frei beweglich	gekuppelt	gekuppelt
Platz des Durchleuchters	in der Mitte hinter dem Strahlenschutz	an der linken Ecke des Schirmes	etwas links von der Mitte des Schirmes	an der rechten Ecke des Schirmes
Ergebnis der Strahlenschutzmessungen:				
Linke Achsel	1 mr/Stde	19 mr/Stde	25 mr/Stde	< 2 mr/Stde
Rechte Achsel	2 »	4 »	12 »	< 2 »
Kragen	3 »	3 »	—	—
Linkes Handgelenk, Unterseite	3 »	58 »	120 »	< 2 »
Rechtes Handgelenk, Unterseite	2 »	6 »	12 »	< 2 »
Sternum	3 »	—	—	—
Symphysenhöhe	1 »	15 »	15 »	60 » [1]
Knie[2]	—	80 »	260 »	20 »
Rechter Fuss[2]	2 »	175 »	35 »	—

[1] Am umlegbaren Universalgerät gemäss Abb. 5 befanden sich die in Symphysenhöhe befestigten Messkammern im allgemeinen unter oder zwischen den beiden am Leuchtschirm befestigten kurzen Bleigummilappen.

[2] Die durch die Röhrenhaube kommende stark geschwächte Primärstrahlung trägt kaum zu den angegebenen Messwerten bei.

leuchtung erhält, wurden eine Anzahl Dosismessungen bei (normalen) Dickdarmkontrasteinläufen an Universalgeräten verschiedener Konstruktion durchgeführt. Der Durchleuchter trug an jedem Messpunkt eine Anzahl Jonisationskammern (SIEVERT und WALSTAM). Alle Durchleuchtungen wurden von demselben Arzt ausgeführt, um unnötige arbeitstechnische Variationen zu vermeiden. Bei den Untersuchungen an den umlegbaren Universalgeräten trug der Durchleuchter eine Strahlenschutzschürze. Die Jonisationskammern, die durch die Strahlenschutz-

schürze abgeschirmt worden wären, wurden oberhalb der Schutzschürze an den entsprechenden Stellen befestigt.

Die Abb. 2 bis 5 zeigen die Strahlenschutzanordnungen der verschiedenen Universalgeräte. Abb. 3 bis 5 zeigen Universalgeräte mit Motorumlegung.

Tabelle I enthält die aus Gesichtspunkten des Strahlenschutzes wesentlichen Angaben über die Schutzanordnungen und die Messresultate bei einer Durchleuchtungsspannung von 80 kV und einem Röhrenstrom von 3 mA. Die Feldgrösse betrug im Mittel etwa 200 cm². Jede Messerie umfasste 3 bis 7 Kontrasteinläufe. Die Resultate sind in Milliröntgen pro Stunde Durchleuchtung angegeben. Der Durchleuchter verliess den Röntgenraum während der Aufnahmen. Die Einlaufskanne wurde vom Durchleuchter bedient. Palpation mit den Händen kam bei diesen Untersuchungen absichtlich nicht vor. Ein- und Ausschaltung der Röntgenröhre wurde im Bedienungsraum durch eine Röntgenschwester vorgenommen.

Die erste Untersuchung in dieser Serie wurde am Kreiskrankenhaus in Falun an einem Trochoskop schwedischen Fabrikates (ähnlich Abb. 2) und einem umlegbaren Universalgerät (ähnlich Abb. 4) durchgeführt. In Tabelle II sind die Strahlenschutzanordnungen dieser Geräte und die Messresultate dargestellt.

Tabelle II

	Trochoskop schwedischen Typs (ähnlich Abb. 2)	Umlegbares Universalgerät (ähnlich Abb. 4, Spiegelbild)
Strahlenschutzanordnungen:		
Grösse des Leuchtschirmes mit Rahmen		
Breite	45 cm	49 cm
Tiefe	55 cm	52 cm
Am Leuchtschirm befestigter Bleigummilappen		
Breite	43 cm	nicht
Länge	43 cm	vorhanden
Schutzschild vor dem Durchleuchter		
Breite	60 cm	nicht
Höhe vom Boden	10—95 cm	vorhanden
Röhre-Leuchtschirm	frei beweglich	gekuppelt
Platz des Durchleuchters	in der Mitte hinter dem Strahlenschutz	an der rechten Ecke des Schirmes
Ergebnis der Strahlenschutzmessungen:		
Rechte Achsel	< 2 mr/Stde	2 mr/Stde
Rechtes Handgelenk, Unterseite	< 2 »	40 »
Symphysenhöhe	< 2 »	150 »
Rechter Fuss	10 »	40 »

Alle Messungen zeigen, dass die untersuchten Trochoskope schwedischen Typs aus Strahlenschutzgesichtspunkten günstiger sind als die untersuchten umlegbaren Universalgeräte.

Die grosse Variation der Messresultate für Fuss und Knie des Durchleuchters bei den umlegbaren Universalgeräten beruht hauptsächlich darauf, dass verschiedene Konstruktionsteile die Sekundärstrahlung mehr oder weniger abschirmen.

Oft wird die Ansicht geäussert, dass die Strahlengefährdung des Untersuchers bei Durchleuchtungsgeräten, deren Leuchtschirm unabhängig von der Röhre bewegt werden kann, grösser ist als bei Geräten, bei denen Röntgenröhre und Leuchtschirm gekuppelt sind (Deutsche Normen; ERNST; GLOCKER). Bei den beiden Trochoskopen schwedischen Typs konnten Leuchtschirm und Röhre unabhängig voneinander bewegt werden. Trotzdem zeigten hier die an den Achseln und den Handgelenken des Durchleuchters befestigten Messkammern nur zwischen 1 und 3 mr pro Stunde Durchleuchtung. Für einen mit dieser Arbeitsweise vertrauten Durchleuchter ist nämlich die Gefahr, dass er sich der Nutzstrahlung aussetzt, sehr gering, während andrerseits die Arbeit dadurch, dass nur die Röhre bewegt zu werden braucht, erleichtert wird. Erheblich höhere Strahlungsdosen zeigten die an den gleichen Punkten befestigten Messkammern bei der Durchleuchtung mit den umlegbaren Universalgeräten (ausgenommen Gerät gemäss Abb. 5, da hier die Grösse des Leuchtschirmes inkl. Rahmen ungewöhnlich gross ist). Bei zwei von diesen Geräten waren Leuchtschirm und Röhre gekuppelt, während bei dem schwedischen Gerät Leuchtschirm und Röhre frei gegeneinander bewegt werden konnten. Bei den umlegbaren Universalgeräten gemäss Abb. 3 und 4 waren die linke Achsel und das linke Handgelenk des Durchleuchters erheblich mehr strahlengefährdet als die rechte Achsel und das rechte Handgelenk, da der Untersucher sich wegen der Lage des Bedienungsarmes an der linken Seite des Schirmes aufhalten musste.

Für die freundliche Erlaubnis diese Messungen an Geräten der vor Ihnen geleiteten röntgendiagnostischen Abteilungen ausführen zu dürfen wollen wir Herrn Prof. K. LINDBLOM (Karolinska sjukhuset, Stockholm), Herrn Doktor H. SAHLSTEDT (Kreiskrankenhaus, Falun), Herrn Dr. med. K. G. SUNDBERG (Kreiskrankenhaus, Södertälje) und Herrn Prof. C. WEGELIUS (Epidemiekrankenhaus der Stadt Stockholm) unseren besten Dank sagen.

ZUSAMMENFASSUNG

Vergleichende Strahlenschutzmessungen zeigen, dass die Strahlenschutzverhältnisse bei der Untertischdurchleuchtung an sämtlichen untersuchten umlegbaren Universalgeräten bedeutend ungünstiger sind als die Strahlenschutzverhältnisse an Trochoskopgeräten schwedischen Typs. Während der Durchleuchter bei einem solchen Gerät mit

Strahlendosen von 1 bis 3 mr pro Stunde Durchleuchtung getroffen wurde, sind die entsprechenden Werte bei den untersuchten umlegbaren Universalgeräten 2 bis 260 mr/Stunde.

SUMMARY

Comparative measurements show that the protection from roentgen radiation afforded in under-couch screening is much less effective in all universal tilting couches than is the case with the Swedish Trochoscope. Whereas with the latter the operator carrying out screening was exposed to radiation doses of 1 to 3 mr per hour, the corresponding values for the universal tilting couch apparatus were 2 to 260 mr per hour.

RÉSUMÉ

Des mesures comparatives montrent que la protection contre les rayons roentgen au cours de la radioscopie avec le tube sous la table est beaucoup moins efficace avec toutes les autres tables basculantes universelles qu'avec le Trochoscope suédois. Alors qu'avec celui-ci, l'opérateur faisant une radioscopie est exposé à une dose de radiation de 1 à 3 mr par heure, les valeurs correspondantes pour l'appareil à table basculante universelle sont de 2 à 260 mr par heure.

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IRRADIATION OF SKIN TUMOURS DURING PURE OXYGEN INHALATION

by

K. A. Hultborn and *A. Forssberg*

This communication is concerned with the trial irradiation of skin tumours during the inhalation of pure oxygen by the patient. The considerations behind the procedure will first be presented in a form which is valid for roentgen therapy.

Experimental research in radiobiology made clear long ago that the action of ionizing radiation proceeds in two different ways. The deleterious action on the cells is partly caused by direct 'hits' by the ionizing particles on sensitive cell-elements. In addition, an appreciable amount of damage is caused by intermediate split products of the irradiated water which makes up the major part of the cells. An extensive literature covers the theoretical and experimental aspects of these irradiation effects (*vide* GRAY (1) for a survey of the details).

Some considerations of importance to an understanding of the application of this research work to practical problems will be stressed. The deleterious split products, formed by the irradiation of water, appear to be very short-lived and strongly oxidizing radicals. The formation of these radicals is appreciably increased in the presence of oxygen. On irradiation of micro-organisms, for example, which are able to live under aerobic as well as anaerobic conditions, one finds that for a given dose the number of cells killed is about two to three times higher in the presence of oxygen than in a nitrogen atmosphere.

Submitted for publication, June 17, 1954.

The principle that increased oxygen tension during the irradiation runs parallel with increased damage is universal. A large number of observations suggest, that the quantitative correlation between the biologic effect and oxygen tension may be roughly given as follows: If the biologic effect (damage) at zero oxygen tension (complete anaerobiosis) be expressed as 1, the maximum effect obtained by increasing the oxygen supply may be denoted by a figure around 3. On the basis of theoretical considerations it is deduced that a maximal increase in effect by a factor of 4 is possible; in experimental biologic work, this, however, is rarely attained.

The following facts are now of basic importance. First, the percental increase in biologic effect will be very high when the oxygen supply is varied between zero concentration and a concentration similar to that in the normal healthy cells. Secondly, an increase of the oxygen supply above that of the average value for normal cells does not cause much additional damage.

Tumours are generally characterized by an anaerobic metabolism concomitant with a low oxygen concentration of the tumour cells. It appears from these considerations that, provided the oxygen concentration of the tumour cell could be experimentally increased, even on a rather limited scale, the damage to the tumour would be appreciably increased, but that to the surrounding normal tissue only slightly increased. GRAY et al. (2) showed this to be experimentally possible in Ehrlich ascites tumour simply by giving the animals pure oxygen to breathe shortly before, and during, the irradiation of the inoculated tumours.

It appears that the principle outlined above will be valid only if the state of the tumour makes possible an increase of the oxygen tension within it. It was found, in GRAY's investigation, that old tumours responded less favourably to this mode of treatment, probably because of difficulties in obtaining a sufficient oxygen flow through the disordered vascular system.

We also have another basis for these trials. HULTBORN (3) studied the effect of preoperative irradiation in operation specimens of carcinoma of the rectum. He found in his histopathologic studies that those parts of the growth which undergo destruction first, consist of the spearheads of the cancerous invasion, whereas those that survive are situated nearer to the site of origin, namely, in the mucosa and submucosa. In a few cases he was able to show distinct evidence of varying degrees of effect in cancerous offshoots directed towards the deeper tissues, most pronounced in the most peripheral parts. HULTBORN continued: "Although I have no satisfactory explanation of the fact that cancer seems to undergo destruction first in the deeper layers of the bowel wall and in the extrarectal tissue, it is conceivable that the malignant cells in the

invasion area are proliferating more vigorously and are therefore the most radiosensitive. The stroma reaction might also be expected to be most pronounced in the periphery, with its better vascularization." We now believe that the explanation of this difference in radiosensitivity lies in a higher oxygen concentration in the offshoots in the peripheral part of the tumour.

In four cases we compared the effect on the tumour and the surrounding normal skin after irradiation with and without inhalation of pure oxygen. In most cases we gave lower doses than usual — this because we felt that there would be better chances of observing any eventual differences in the effects of irradiation.

Case 1. RH 36/54. Female, aged 66. A microscopically verified intra-epidermal basal cell carcinoma with spinocellular structures and having a diameter of 6.5 cm, was present over the sacro-iliac joint. Together with the adjacent normal skin, it was divided into two irradiation fields, the two halves of the tumour being identical in appearance, thickness and size. Four doses of 700 r, measured on the skin with ionisation chambers, were given to each field. One field was irradiated in the mornings without oxygen inhalation; the other in the afternoons during oxygen inhalation at atmospheric pressure. At each treatment the non-irradiated field was shielded with 2 mm lead (see Table I).

Table I

Field	Date	Inhalation of Pure Oxygen before Start of Treatment Minutes	kV	mA	Field Size cm²	Irradiation Time per Day Minutes	Focus—Skin Distance Centimeters	Filter mm Al	Surface Dose r	Surface Dose, Measured with Ionisation Chambers r	Total Dose per Field r
I	25/1	—	135	10	25	11.9	40	4	700	682	700
I	26/1	—	135	10	25	12.5	40	4	700	683	1,400
I	27/1	—	135	10	25	12.5	40	4	700	671	2,100
I	28/1	—	135	10	25	12.5	40	4	700	646	2,800
									2,800	2,682	
II	25/1	16	135	10	25	11.9	40	4	700	662	700
II	26/1	32	135	10	25	12.5	40	4	700	634	1,400
II	27/1	25	135	10	25	12.5	40	4	700	638	2,100
II	28/1	26	135	10	25	12.5	40	4	700	654	2,800
									2,800	2,588	

The reaction was most pronounced in the field irradiated during the inhalation of oxygen. The resulting ulceration healed very slowly by epithelialization from the periphery; that in the tumour zone itself showed especially slow healing. In the field irradiated without oxygen inhalation the reaction was less pronounced, and the ulceration healed rapidly by epithelialization from multiple small islets (Figs. 1 and 2).

It would thus seem that the inhalation of oxygen amplified the effect of irradiation, especially in the tumour zone.

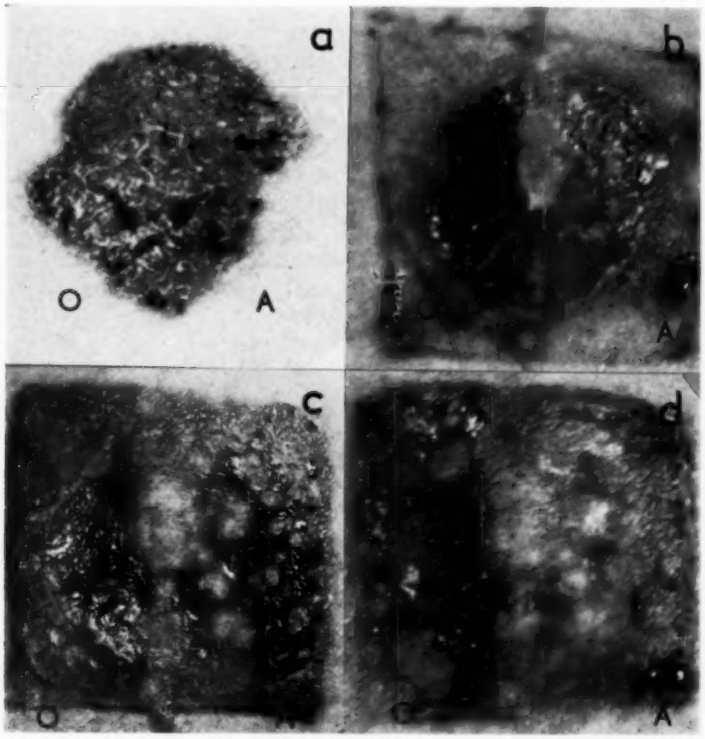


Fig. 1. Case 1. A = air. O = oxygen. a. Before treatment. b. Twenty-three days after treatment. c. Thirty days after treatment. d. Thirty-four days after treatment.

Case 2. RH 794/32. Male, aged 59. The patient had undergone repeated treatment over a period of many years for a large number of multiple intra-epidermal carcinomas. In this trial we irradiated six tumours of a similar thickness and appearance in the right gluteal region (Fig. 4 a) and four similar tumours on the ventral surface of the thorax. In addition, a more extensive tumour above the left mammilla was treated, being divided into two identical fields (Figs. 3 a and b).

On 1 March, in the afternoon, five of the small skin carcinomas were irradiated during the inhalation of oxygen, two receiving 1,000 r each and three 3,000 r each. The large tumour received a dose of 1,500 r to one field, the other field being protected with 2 mm lead. On 2 March, in the morning, the other five small skin carcinomas were irradiated without oxygen inhalation, the doses being 1,000 r to each of two and 3,000 r to each of three. To the previously untreated field of the large tumour, 1,500 r was given, with protection of the other field by 2 mm lead (Table II).

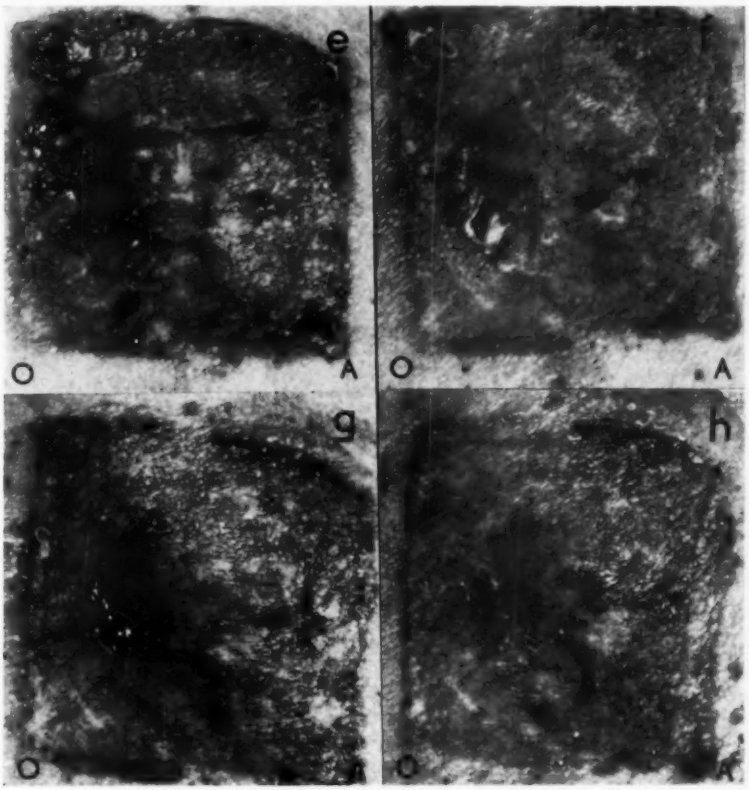


Fig. 2. Case 1. A = air. O = oxygen. e. Thirty-seven days after treatment. f. Forty-seven days after treatment. g. Fifty-five days after treatment. h. Sixty-seven days after treatment.

Examination on 4 April showed no demonstrable difference between the reactions in the fields irradiated with 1,000 r with and without oxygen inhalation. The large tumour, which had been divided into two fields, presented no appreciable differences in the area involved; the surrounding normal skin, however, showed a pronounced reaction, consisting of more marked brown pigmentation and desquamation in the field irradiated during oxygen inhalation (Fig. 3 c). With regard to the six small skin carcinomas that received 3,000 r each, there was a considerable difference in the effect of irradiation between those treated with and those treated without concomitant oxygen inhalation. In each of the three irradiated during inhalation, a large ulcerous area had developed in the tumour zone; of the three treated without oxygen inhalation, however, two showed only a small ulcerous area and the other none at all (Fig. 4 b).

Table II

Field	Date	Inhalation of Pure Oxygen before Start of Treatment of Field 79 Minutes	kV	mA	Field Size cm^2	Irradiation Time—Minutes	Focus—Skin Distance Centimeters	Filter mm Al	Surface Dose r
79	1/3	35	49	10	6	$1\frac{24}{60}$	10	0.25	3,000
80	1/3	35+	49	10	6	$1\frac{24}{60}$	10	0.25	3,000
81	1/3	35+	49	10	6	$1\frac{24}{60}$	10	0.25	3,000
82	1/3	35+	49	10	6	$\frac{28.1}{60}$	10	0.25	1,000
83	1/3	35+	49	10	6	$\frac{28.1}{60}$	10	0.25	1,000
84 a	1/3	35+	49	10	10	$\frac{40.6}{60}$	10	0.25	1,500
84 b	2/3	—	49	10	10	$\frac{40.6}{60}$	10	0.25	1,500
85	2/3	—	49	10	6	$\frac{28.1}{60}$	10	0.25	1,000
86	2/3	—	49	10	6	$\frac{28.1}{60}$	10	0.25	1,000
87	2/3	—	49	10	6	$1\frac{24}{60}$	10	0.25	3,000
88	2/3	—	49	10	6	$1\frac{24}{60}$	10	0.25	3,000
89	2/3	—	49	10	6	$1\frac{24}{60}$	10	0.25	3,000

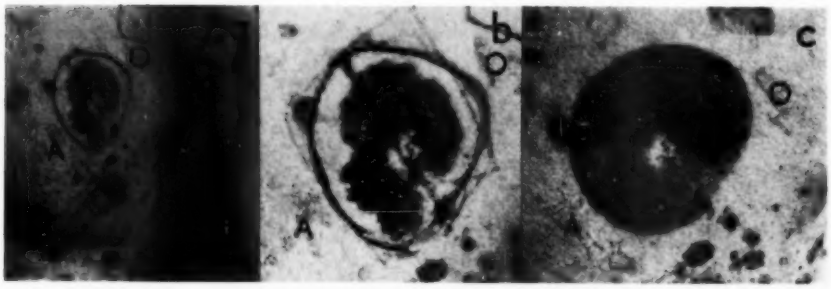


Fig. 3. Case 2. A = air. O = oxygen. a and b. Fields 84 a and 84 b, before treatment. c. Same fields thirty-three days after treatment. Radiodermatitis in the upper right segment of the irradiated area.

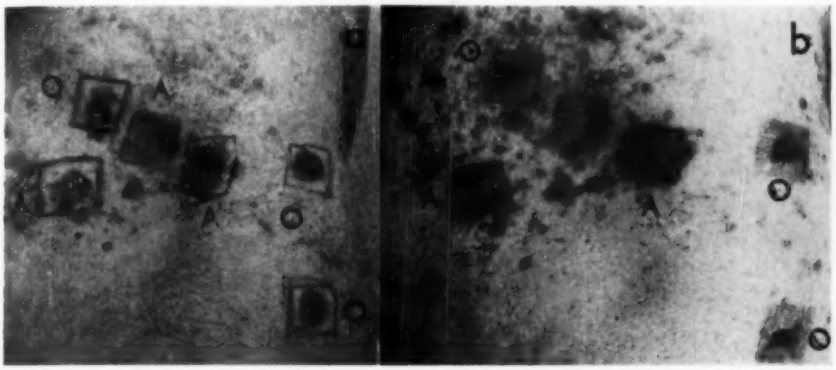


Fig. 4. Case 2. A = air. O = oxygen. a. Fields 79—81 and 87—89 before treatment, b. Same fields thirty-three days after treatment. The three fields showing the greatest ulceration were irradiated during concomitant oxygen inhalation.

Concomitant oxygen inhalation in this case also appears to have amplified the effect of irradiation, particularly in the tumour area itself.

Case 3. RH 1738/54. Male, aged 50. Skin tumour of hairy part of left axilla showing typical appearance of basal cell carcinoma, measuring 1.5 by 2.5 cm, with a thickness of about 5 mm. Together with the surrounding normal skin, it was divided into two irradiation fields, in the lateral of which the tumour had its greatest extension and depth. Each field received four doses of 500 r, measured on the skin with ionisation chambers. The lateral field was irradiated during oxygen inhalation in the mornings, the medial field without inhalation, 3 to 5 hours later. At each treatment the non-irradiated field was shielded with 2 mm lead (Table III).

Table III

Field	Date	Inhalation of Pure Oxygen before Start of Treatment Minutes	kV	mA	Field Size cm²	Irradiation Time per Day Minutes	Focus—Skin Distance Centimeters	Filter mm Al	Surface Dose r	Surface Dose, Measured with Ionisation Chambers r	Total Dose per Field r
I	16/3	40	140	10	5	9.6	40	4	500	500	500
I	17/3	40	140	10	5	9.6	40	4	500	522	1,000
I	18/3	29	140	10	5	9.6	40	4	500	513	1,500
I	19/3	40	140	10	5	9.6	40	4	500	499	2,000
									2,000	2,024	
II	16/3	—	140	10	5	9.6	40	4	500	517	500
II	17/3	—	140	10	5	9.6	40	4	500	526	1,000
II	18/3	—	140	10	5	9.6	40	4	500	499	1,500
II	19/3	—	140	10	5	9.6	40	4	500	499	2,000
									2,000	2,041	

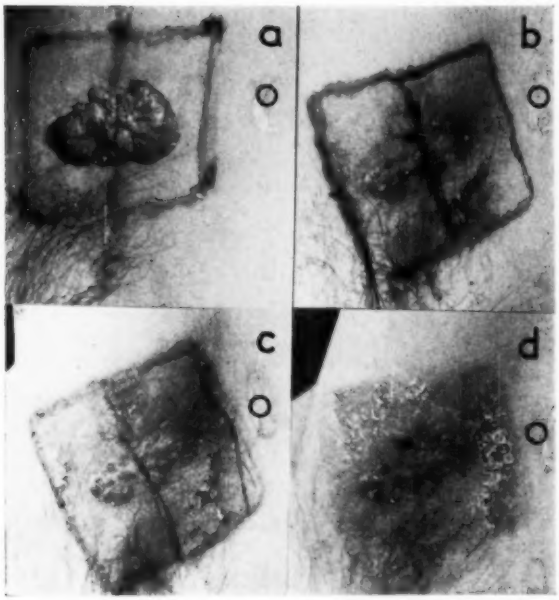


Fig. 5.

Fig. 6.

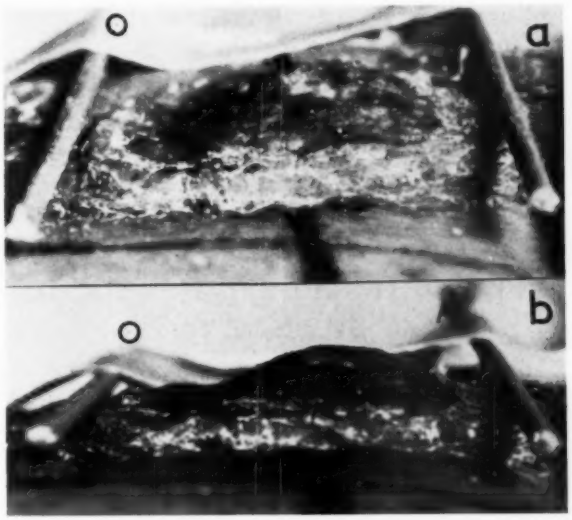
Fig. 5. Case 3. a. Before treatment. b. Thirty-two days after treatment. c. Thirty-eight days after treatment. d. Forty-five days after treatment.

Fig. 6. Case 4. Before treatment (photograph taken directly from above). The tumour had the same thickness throughout its area.

The tumour regressed at the same rate in the two fields, but on 26 April and 3 May, the regression seemed to be most pronounced in the field irradiated during concomitant oxygen inhalation. On 20 April and particularly on 26 April, the skin of the field treated during inhalation showed a marked reaction in the form of more pronounced pigmentation, dryness and desquamation (Fig. 5).

Case 4. RH 2868/54. Female, aged 83. Long-standing verruciform tumour on the lateral aspect of the right thigh. Five years previously it had commenced to grow in size and ulcerate; it was now bleeding slightly and measured 3 × 5 cm with a thickness of 4 mm (Fig. 6). Biopsy disclosed a pigmented epithelioma, probably arising from the sweat glands, which had manifestly undergone malignant transformation. Together with the adjacent normal skin, it was divided into two irradiation fields, with the two halves of the tumour identical in appearance, thickness and size. Four doses of 500 r, measured on the skin with ionisation chambers, were given to each field. One field was irradiated in the morning without oxygen inhalation, the other in the afternoon during oxygen inhalation at atmospheric pressure. At each treatment the non-irradiated field was shielded with 2 mm lead (Table IV).

On 22 May the portion irradiated during concomitant inhalation of oxygen showed a considerably greater decrease in thickness than the other half and by 4 June the difference was further accentuated (Figs. 7 a and b). No skin reaction had occurred in the field irradiated without concomitant inhalation, and in the other field only a slight erythema continuous to the tumour, was present.



Figs. 7 a and b. Case 4. A = air. O = oxygen. Twenty-seven days after treatment. The borders of the tumour are marked by wooden pegs (photographs taken obliquely from above and directly from the side); the half treated during concomitant oxygen inhalation is now depressed — some of it below the level of the surrounding skin — whereas the other half shows less regression.

Table IV

Field	Date	Inhalation of Pure Oxygen before Start of Treatment Minutes	kV	mA	Field Size cm²	Irradiation Time per Day Minutes	Focus—Skin Distance Centimeters	Filter mm Al	Surface Dose r	Surface Dose, Measured with Ionisation Chambers	Total Dose per Field
I	5/5	—	144	10	15	8.3	40	4	500	543	500
I	6/5	—	144	10	15	8.3	40	4	500	468	1,000
I	7/5	—	144	10	15	8.3	40	4	500	523	1,500
I	8/5	—	144	10	15	8.3	40	4	500	543	2,000
									2,000	2,077	
II	5/5	29	144	10	15	8.3	40	4	500	541	500
II	6/5	36	144	10	15	8.3	40	4	500	536	1,000
II	7/5	40	144	10	15	8.3	40	4	500	546	1,500
II	8/5	26	144	10	15	8.3	40	4	500	520	2,000
									2,000	2,143	

In this case oxygen inhalation appears, therefore, to have amplified the effect of irradiation in the tumour tissue without having appreciably increased the radiosensitivity of the normal skin.

The present investigation is still in its opening phase and we are aware that no conclusions should yet be drawn from these few trials. Since, however, our observations so far are encouraging enough to warrant further trials, we feel justified in presenting this preliminary report. We propose to continue as before with human skin carcinoma, for in this form it is easiest to study the biologic effect both in the tumour tissue and in the normal skin. Moreover, we hope to be able soon to carry out trial irradiation during the concomitant inhalation of pure oxygen at a positive pressure of 0.5 to 1 atmosphere in the hope of obtaining greater effects.

SUMMARY

Following a brief survey of the theoretical considerations, four cases of skin tumours treated by trial irradiation with the concomitant administration of pure oxygen, are presented. The results, which are encouraging, are discussed. It is emphasized that the communication is in the nature of a preliminary report.

ZUSAMMENFASSUNG

Nach einem kurzen Überblick über die theoretischen Erwägungen werden 4 Fälle mit Hauttumoren geschildert, die versuchsweise mit Bestrahlung unter gleichzeitiger Zuführung reinen Sauerstoffes behandelt worden sind. Die Ergebnisse, welche ermutigend sind, werden besprochen. Es wird hervorgehoben, dass die Mitteilung den Charakter eines vorläufigen Berichtes hat.

RÉSUMÉ

Après un bref rappel de considérations théoriques, les auteurs présentent quatre cas de tumeurs cutanées traitées par une irradiation d'épreuve avec administration simultanée d'oxygène pur. Ils examinent les résultats qui semblent encourageants. Ils insistent sur le fait que cette communication est une note préliminaire.

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THE PROTECTIVE EFFECT OF CYSTEAMINE ON YOUNG MICE EXPOSED TO ROENTGEN RAYS

by

Arne Nelson

The rapid development of atomic weapons since 1945 when the first atomic bombs were dropped in Japan has rendered protection from the injurious effects of ionizing radiation of great importance. Research has been concentrated on finding, firstly a specific therapy for radiation injuries and secondly a means to reduce the effect of ionizing radiation (SELLE 1951). In the first case exertions have not led to any obvious result, even if there have been comparatively optimistic reports concerning the effect of certain splenic extracts.

A considerable number of substances have been investigated in order to find a means of protection against the effects of ionizing radiation. RUGH (1953) inter alios made a survey of these investigations. The best results have been achieved with substances containing SH-groups, *e. g.* cysteine (PATT, TYREE, STRAUBE and SMITH 1949, PATT, SMITH, TYREE and STRAUBE 1950, GOLDIE, TARLETON and HAHN 1951), as well as cysteamine, $HS - CH_2 - CH_2 - NH_2$ (= β-mercaptoethylamine = Bécaptan) and the corresponding disulfide (cysteine amine) (BACQ et al. 1952).

BACQ exposed groups of mice weighing 19 to 20 g to radiation giving an initial dose of 700 r. Practically all the control animals died within 5 to 15 days. On the contrary, 97 % of mice which received an intraperitoneal injection of 3 mg cysteamine 1 to 3 min. previous to the irradiation, survived. Mice protected by means of cysteamine had to be given a radiation dose of about 1,300 r in order to obtain the same mortality curve produced by 700 r without any cysteamine protection. Cysteamine becomes rapidly excreted and if the injection was given 1 hour before the irradiation, the effect of protection had practically dis-

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appeared. BACQ (1952) obtained an optimal protective effect with cysteamine in a series of tests by its injection immediately before, and in a second series 30 min. before, the irradiation. In the case of a test with *cysteine amine* he obtained an optimal effect by its injection immediately before the irradiation. In a test on rats exposed to a dose of radiation of 700 r (LAMBERT, MARSIN and MANDART 1952) 40 % of those injected with cysteamine survived, whereas all the controls died.

As a stage in a series of investigations on chemical substances possessing protective effects against ionizing radiation, the writer has endeavoured to reproduce some of BACQ's tests on mice with the difference that young mice have been used as test animals, and that in addition to the time of survival, the body weight of the animals has also been used as a criterion.

Material and Methods

White male mice of pure inbred stock weighing about 14 g were irradiated in groups of 10 in a plastic holder. The radiation conditions were as follows: 145 kVp, 6 mA, 1 mm Al, F. T. D. 38 cm, and 76 r/min.

The tests were carried out in two series. In the first one the mice were divided into 5 groups of 20, and 4 groups were irradiated with 600 r, 800 r, 1,000 r, and 1,200 r, respectively. An unirradiated group served as a control. In each group half of the mice received an intraperitoneal injection of 3 mg cysteamine. The irradiated mice received the injection immediately before irradiation. In the second series, groups of 50 mice were exposed to 600 r, 800 r and 1,000 r respectively. Every group exposed was divided up into 5 subgroups, each containing 10 mice, which were given the following treatment:

a) Cysteamine injection immediately before irradiation.
b) » » 15 min. » »
c) » » 30 min. » »
d) » » 1 hour » »
e) No cysteamine injection.

A control group of 20 mice was treated as in the previous series. In both of these test series each mouse was weighed 3 times per week and every morning the number of surviving mice was noted.

Result

A. *The first test series*

1. General condition. Immediately after the injection the mice which had received cysteamine perspired, their fur became sticky and one mouse died during the irradiation, probably owing to the effects of the cysteamine.

2. Time of Survival. As will be seen from Fig. 1 a and Table 1 all the mice in both controls as well as 9 out of 10 in both series, which were irradiated with 600 r, survived. After receiving 800 r all the mice

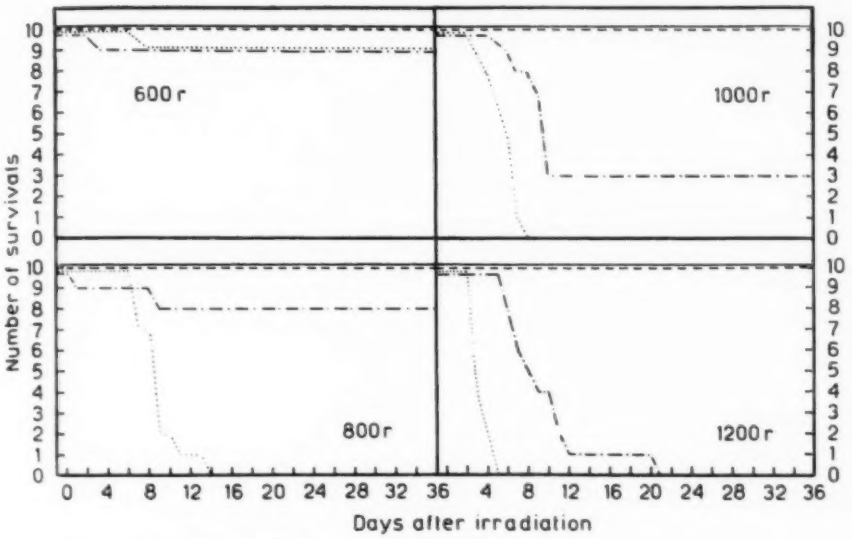

Fig. 1 a. First test. Number of survivals.
Non-irradiated controls
» » » , cysteamine injected
Irradiated groups only
» » , cysteamine injected

which had not been treated with cysteamine died within 14 days (average time of survival 8.6 days), while of those receiving cysteamine 8 out of 10 survived. With a dosage of 1,000 r, all those not treated with cysteamine within 8 days (average time of survival was 5.6 days) died. Of those treated with cysteamine, 3 out of 10 survived. All mice treated with 1,200 r died, though the time of survival for those treated with cysteamine was longer than the others (average time of survival was 9.5 and 3.6 days respectively).

Table 1

First test: Rate and time of survival

Effect of cysteamine injected in young mice immediately before irradiation

Dose in r	Rate of survival (groups of ten)		Average time of survival in days	
	No injection	Injection of cysteamine	No injection	Injection of cysteamine
600	9	9	—	—
800	0	8	8.6	—
1,000	0	3	5.6	—
1,200	0	0	3.6	9.5
control	10	10	—	—

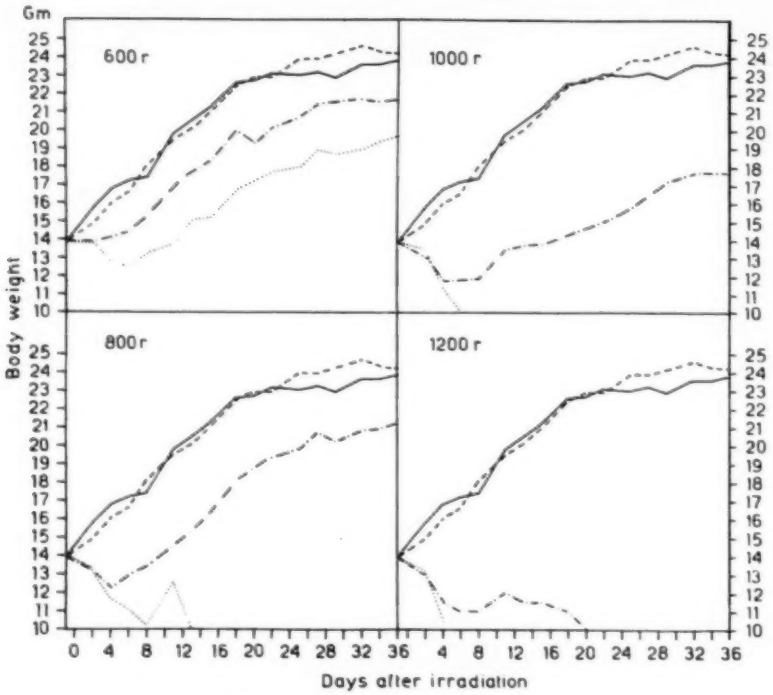

Fig. 1 b. First test. Average body weight.

3. Changes in weight. As will be seen from Fig. 1 b the two control groups showed a normal increase in the average weight, except in the case of the mice injected with cysteamine during the first week, when the increase was slightly delayed. In the groups irradiated there is a primary decrease in weight, which is more pronounced after about 6 days, when the weight again increases in the mice that survive. Nevertheless this increase never comes up to the weights of the control groups. The primary decrease in weight mentioned is not to be found in the groups exposed to 600 r which have been injected with cysteamine. Practically speaking the average weight of the mice injected with cysteamine is considerably greater during the whole time of observation than is the case of those corresponding to the mice not injected with cysteamine. The average weight of those surviving is reversed, as compared with the dose, *i. e.* the greater the dose, the less the average weight.

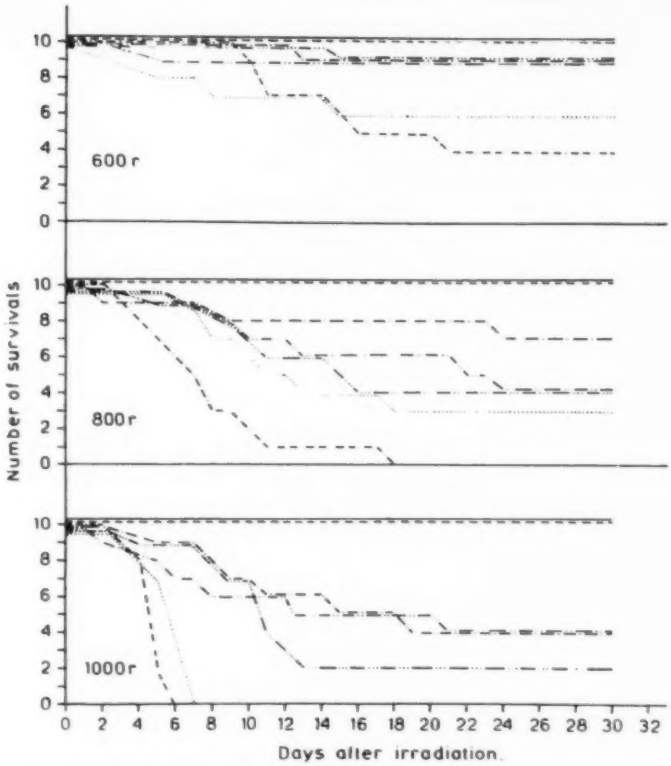

Fig. 2 a. Second test. Number of survivals.

Non-irradiated controls.
» » » , cysteamine injected
Irradiated groups without cysteamine injection
» » , cysteamine injection immediately before irradiation
» » , cysteamine injection 15 min. before irradiation
» » , cysteamine injection 30 min. before irradiation
» » , cysteamine injection 1 hr. before irradiation

B. *The Second Test Series*

1. Time of Survival. As will be seen from Fig. 2 a and Table 2, when mice were exposed to an irradiation of 600 r without any cysteamine injection, only 4 out of 10 survived, whereas the number of survivors after a cysteamine injection became 9 out of 10, if this

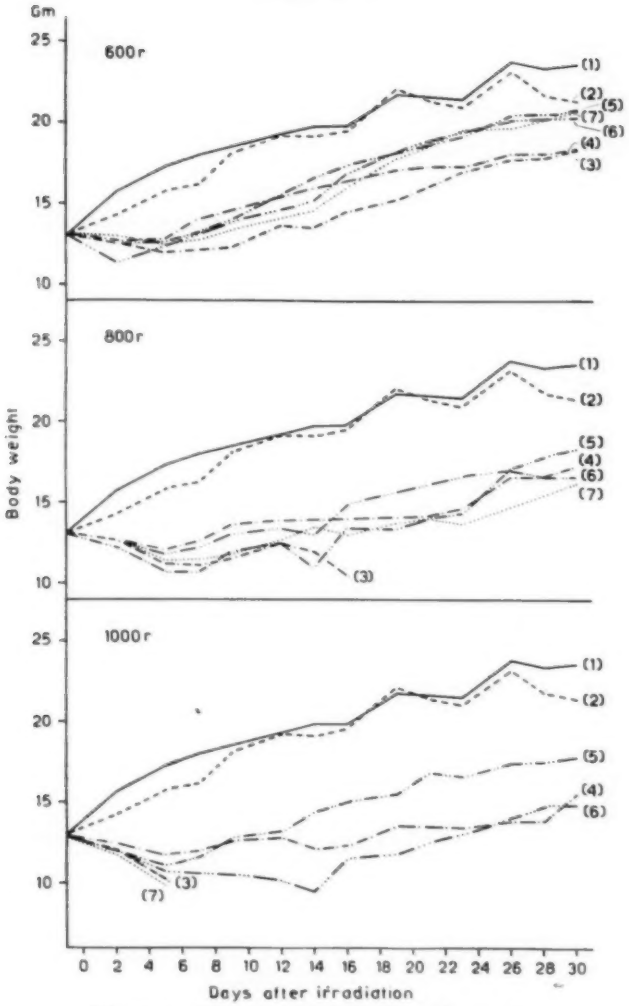

Fig. 2 b. Second test. Average body weight.

was given immediately before (15 min. and 30 min.) the irradiation, whereas only 6 out of the 10 survived if the injection was performed 1 hour previous to the irradiation. If mice were treated with 800 r and received no cysteamine, they did not survive for more than 18 days, the average time of survival being 8.1 days. If the injection was made

immediately before the irradiation, 7 out of 10 survived; if carried out 15 min. and 30 min. before exposure, 4 out of 10 survived; and if performed 1 hour before exposure 3 out of 10 survived.

In the group that had been exposed to 1,000 r, none of the untreated mice and none of those injected with cysteamine 1 hour previously, survived. In the latter cases, however, the time of survival was somewhat longer, on an average 3.7 and 5.9 days respectively. When injections were given immediately before irradiation, 4 out of 10 mice survived; when injections were given 15 min. before, 3 survived; and 30 min. before, 2 out of 10 survived.

Table 2

Second test: Rate and time of survival

Effect of cysteamine injected on young mice at different times before irradiation

Dose in r	Rate of survival (groups of ten)					Average time of survival in days				
		Injection of cysteamine					Injection of cysteamine			
	No injection	Immediately before	15 min. before	30 min. before	1 hr. before	No injection	Immediately before	15 min. before	30 min. before	1 hr. before
600	4	9	9	9	6	—	—	—	—	—
800	0	7	4	4	3	8.1	—	—	—	—
1,000	0	4	3	2	0	3.7	—	—	—	5.9
Total	4	20	16	15	9					

2. Changes in weight. (Fig. 2 b.) As in the case of the first test series, the control group treated with cysteamine increased slowly in weight during the first week, subsequently to continue in the control group which had not been treated with cysteamine. The divergence recorded in these two curves during the last few days in the time of observation seemed to be caused by factors other than those of the test. In the group exposed to 600 r, the weight of the mice treated with cysteamine was definitely above those not treated with this compound. Nevertheless there was a decrease in the groups which received cysteamine immediately before the irradiation and towards the end of the time of observation. Furthermore, the average weights of the groups treated with cysteamine run together, particularly towards the end of the time of observation.

Discussion

As in the tests carried out by the writer of this paper, BACQ's basic tests, which have also been reproduced by LANGENDORFF (1954) et coll., have shown that cysteamine considerably diminishes the effect of ionizing radiation when making animal tests. Practically speaking the mortality and the survival curves in the case of mice exposed to 800 r without

cysteamine were in agreement with corresponding data on mice exposed to irradiation with 1,200 r after cysteamine injections. While all mice solely irradiated with 800 r and 1,000 r died, after an injection of cysteamine there was a survival of 8 out of 10 and 3 out of 10, respectively.

The second test, carried out in order to ascertain how long the effect of the cysteamine lasts, showed that the optimal effect was obtained if the cysteamine was injected immediately before irradiation. A comparatively good effect remained even if the injection was given 15 to 30 min. before the irradiation, whereas the effect remaining after one hour was considerably less, even if significant. BACQ maintains that cysteamine possesses low toxicity. Nevertheless from the tests under consideration, it seems clear that cysteamine has an immediate shock-like effect on mice and that they are obviously affected for about 1 hour. Even the inhibitory effect upon growth indicated by the weight, shown in both tests during the first week in the control groups injected with cysteamine as compared with the groups not given cysteamine, indicates a toxic effect.

Experimental investigations, the results of which have been confirmed from several quarters, have shown that cysteamine produces a considerable weakening of the injurious biologic effect of ionizing radiation, but that it possesses comparatively marked toxicity and its action is short-lived. This causes considerable hesitation in giving an opinion upon the practical value of cysteamine as a remedy against the biologic effects of ionizing radiation.

Acknowledgement

The irradiations were performed at the Institute of Radiophysics, Stockholm, for which I wish to express my thanks to Prof. R. SIEVERT and Dr. ARNE FORSSBERG.

SUMMARY

The protective effect of cysteamine against ionizing radiation has been investigated in young mice.

Observations upon the weight and time and rate of survival suggested that cysteamine afforded a good protective effect if given about 30 minutes before a dose of irradiation of up to 800 r and was also of some value when this amounted to 1,000 r.

ZUSAMMENFASSUNG

Die Schutzwirkung des Cysteamines gegenüber jonisierender Strahlung ist an jungen Mäusen untersucht worden.

Beobachtungen des Gewichtes, der Zeit des Überlebens und der Anzahl der Überlebenden ergeben, dass Cysteamin eine gute Schutzwirkung erbietet, falls es etwa 30 Minuten vor der Bestrahlung mit Dosen bis zu 800 r gegeben wird, und dass es auch bei Dosen bis 1,000 r von gewissem Wert ist.

RÉSUMÉ

L'effet protecteur de la cystéamine contre les radiations ionisantes a été expérimenté sur de jeunes souris.

Les résultats concernant le poids et la durée et le taux de survie font penser que la cystéamine, administrée environ 30 minutes avant une dose d'irradiation allant jusqu'à 800 r, a eu un bon effet protecteur, et a eu aussi quelque effet quand la dose atteignait 1,000 r.

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BOOK REVIEWS

THE CENTRAL VEINS AND DEEP DURAL SINUSES OF THE BRAIN. An Anatomic and Angiographic Study. By Curt Johanson. 184 pages, 91 figures and 5 tables. Acta radiol. Suppl. 107. Stockholm 1954. Sw. Kr. 25: —.

This work is a description of the central veins and the deep dural sinuses of the brain from an anatomic as well as a radiologic point of view. An account is given of the normal anatomy. The appearance of the veins in intracranial expanding processes in different situations is described.

The material for the study of the normal anatomy consists of 75 brains (autopsy cases) and of 200 angiograms in living subjects with no expanding or atrophic process in the brain. After selective filling with contrast medium, a roentgenologic examination is made of the central veins and deep dural sinuses in cadavers with the brain *in situ*. The roentgenologic observations are checked through dissection, it being possible to remove the brains with no deformation of the contrast-filled vessels. A special analysis is made of the relationship between the basal vein and the tentorial notch.

The visualization of the veins and dural sinuses in carotid angiography is discussed. With the exception of the choroid vein, the central veins of the injected side are consistently visible in the material presented. This also applies to the straight sinus and, in most cases, to the inferior longitudinal sinus.

The author finds that it is possible to distinguish certain constant features and patterns in the central veins and deep dural sinuses of the brain. A number of details which facilitate their identification are described. Variations in the pattern are found but may be recognized as normal variations. Some of these deviations have earlier been erroneously interpreted as indicative of a pathologic process. No difficulty is encountered in identifying the vessels on angiography in different projections, both lateral and anteroposterior. The central veins are situated in constant relation to various landmarks in the skull and to certain structures of the brain. In films in perpendicular projections, these structures may be localized by studying the position of the central veins and the deep dural sinuses. As the arteries, the central veins and the deep dural sinuses are not concomitant, other parts of the brain may be studied in carotid angiography with the help of the veins rather than the arteries.

The pathologic material consists of 103 cases of a supratentorial expanding process and 10 cases of symmetric hydrocephalus caused by stenosis of the aqueduct or an infratentorial expanding process. A report is given of the displacement of the central veins which is compared to that of the arteries. The deflection of the central veins is found to provide additional information to that given by the appearance of the arteries. This applies in particular when the process extends to the lateral ventricle. In some cases of a central expanding process, it may be localized with the help of the appearance of the central veins alone. No displacement of the deep dural sinuses can be demonstrated. It is observed that a tumour may be indicated not only by a deflection of the vessels, but also by an increase in the calibre of an individual vein when a tumour is present in its drainage area. This applies even when no neoplastic circulation can be demonstrated in the tumour. Displacement of the basal vein may be a sign of herniation through the tentorial notch.

The change of the pattern of the central veins in symmetric hydrocephalus indicates dilatation of the lateral ventricles but gives no information about its cause.

In suprasellar and parasellar expanding processes, the displacement of the internal cerebral vein and the septal vein indicates the extent of the process in upward and backward directions and implies that the process is of considerable size. Lateral extension of the tumour may result in displacement of the anterior part of the basal vein.

Frontal and fronto-parietal expanding processes displace the internal cerebral vein across the midline in the same direction as the arteries in the longitudinal fissure, but to a lesser degree. Furthermore, local deformation of the tributaries to the internal cerebral vein may indicate extension of a process to the lateral ventricle.

In parietal and occipital expanding processes, the internal cerebral vein is almost always displaced across the midline and farther than the arteries in the longitudinal fissure.

In temporal expanding processes, including those of the Sylvian fissure and the insula, the position of the process is found to be indicated particularly by deflection and local deformation of the basal vein. It is frequently possible to delimit the process between the basal vein, the middle cerebral artery and its branches.

In central expanding processes (processes of the basal ganglia, intraventricular expanding processes, those of the corpus callosum, and those in the region of the pineal body), the arterial displacement usually shows signs of hydrocephalus or indicates only part of the process. The appearance of the central veins, however, often permits localization of an expanding process to these parts of the brain.

Autoreview.

TEMPORARY UNILATERAL OCCLUSION OF THE PULMONARY ARTERY. A METHOD OF ROENTGEN EXAMINATION OF THE PULMONARY VESSELS. By Björn Nordenström. 148 pages, 56 illustrations. Acta radiol. Suppl. 108. Stockholm 1954. Sw. Kr. 30: —.

In order to obtain the necessary information for the development of a method of roentgen examination a series of experiments on dogs was performed. The circulation of one lung was blocked by means of a rubber balloon attached to a cardiac catheter.

The supplement is divided into four main parts. The first is a general section, chiefly containing accounts of the equipment and technique of occlusion.

Part II describes attempts to utilize the unilateral occlusion for angiography of the vessels of the occluded lung by injection of a contrast medium distal to the occlusion. In this connection different factors of importance in the technique were investigated.

The blood content of the occluded lung was studied by comparison of the vascular calibre in the right and left lungs in antero-posterior roentgenograms and by the recording of densograms by means of an electrokymograph. A decrease in the blood content of the occluded lung was observed. Due to this a considerably reduced amount of a more dilute contrast medium may be used for angiography of the pulmonary arteries distal to the occlusion.

Contrast medium injected distal to an occluded pulmonary artery does not remain unchanged in the vessels. This is due to the physical factors of the contrast medium, the position of the animal, the respiratory movements, transmitted pulsations from the main trunk of the pulmonary artery and retrograde pulsations from the left auricle, as well as dilution of the medium from the bronchial vascular system. The latter factor was studied more closely. Two methods of angiography of the bronchial arteries are described and the communication between the bronchial and pulmonary vessels demonstrated in the living dog. The importance of the bronchial circulation for the circulation in the occluded lung was also studied by employing a method of blocking the bronchial

arterial circulation. Unilateral angiography of the pulmonary arteries of the occluded lung is summarized from the results of the experiments.

In this part the possibility of obtaining selective venograms of the occluded lung is pointed out.

Part III describes attempts to utilize the unilateral occlusion for angiography of the vessels of the non-occluded lung by the injection of contrast medium proximal to the occlusion. The blood content of the non-occluded lung was studied and the adaptation of the pulmonary circulation to a unilateral occlusion is discussed. The development and testing of a method of roentgen examination of the vessels of the non-occluded lung is then described. In these investigations 'contralateral' contrast filling of the pulmonary veins of the occluded lung was observed; the method may be utilized to obtain selective venograms of a lung.

Part IV contains a brief report on examinations of patients during unilateral occlusion of the pulmonary artery. Two cases of arteriovenous aneurysm, one of pulmonary emphysema, one of middle lobe syndrome, and one of infarction are illustrated. Finally, a selective venogram of a lung is shown.

Autoreview.

THE CONVENTIONAL ROENTGENOGRAM IN THE COMMONEST CONGENITAL MALFORMATIONS OF THE HEART AND GREAT VESSELS IN ADULTS AND JUVENILES. By Georg-Fredrik Saltzman. 60 pp. 33 roentgenograms. Acta radiol. Suppl. 114, Stockholm 1954. Sw. Kr. 25.

The work is based on the cases of congenital malformations examined during the period from 1947 to April 1953 at Roentgen Department I, in collaboration with the Heart Clinic, of Södersjukhuset, Stockholm. The patients were both adults and juveniles.

Of the congenital malformations of the heart and great vessels, the following are dealt with: Tetralogy of Fallot, Eisenmenger's complex, valvular pulmonary stenosis, atrial septal defect, ventricular septal defect, patent ductus arteriosus and coarctation of the aorta. The congenital malformations may be combined in various ways; the paper refers, however, only to 'pure' uncomplicated cases.

Most of the signs observed in the conventional roentgenograms in various congenital malformations of the heart and the great vessels are not pathognomonic of the respective malformations. Nevertheless, it is possible to formulate a number of signs, each in itself uncharacteristic, into a syndrome, more or less typical of each particular malformation, in a manner likely to be useful in practical work. As the paper has, above all, been aimed at facilitating the work of the practical roentgen diagnostician, the problems concerned with the differential diagnosis have received special attention.

Throughout the paper an attempt is made to keep to a terminology based upon the patho-anatomic changes which form the foundations for the roentgenologic signs. In order to avoid confusion and misunderstanding, a number of commonly used unanatomic concepts, some of which are no longer acceptable in the light of the improved technique of examination now available, have been discarded.

Autoreview.

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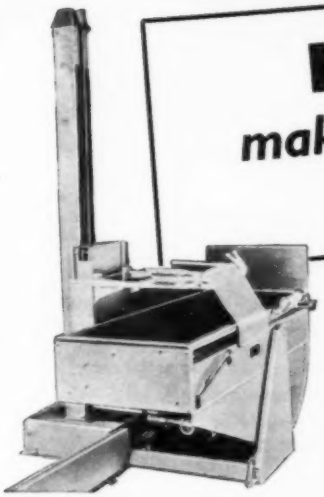

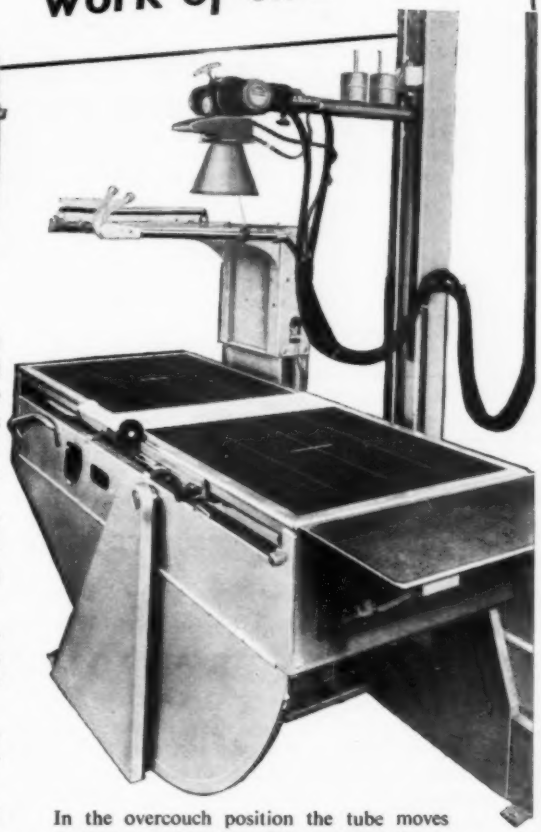

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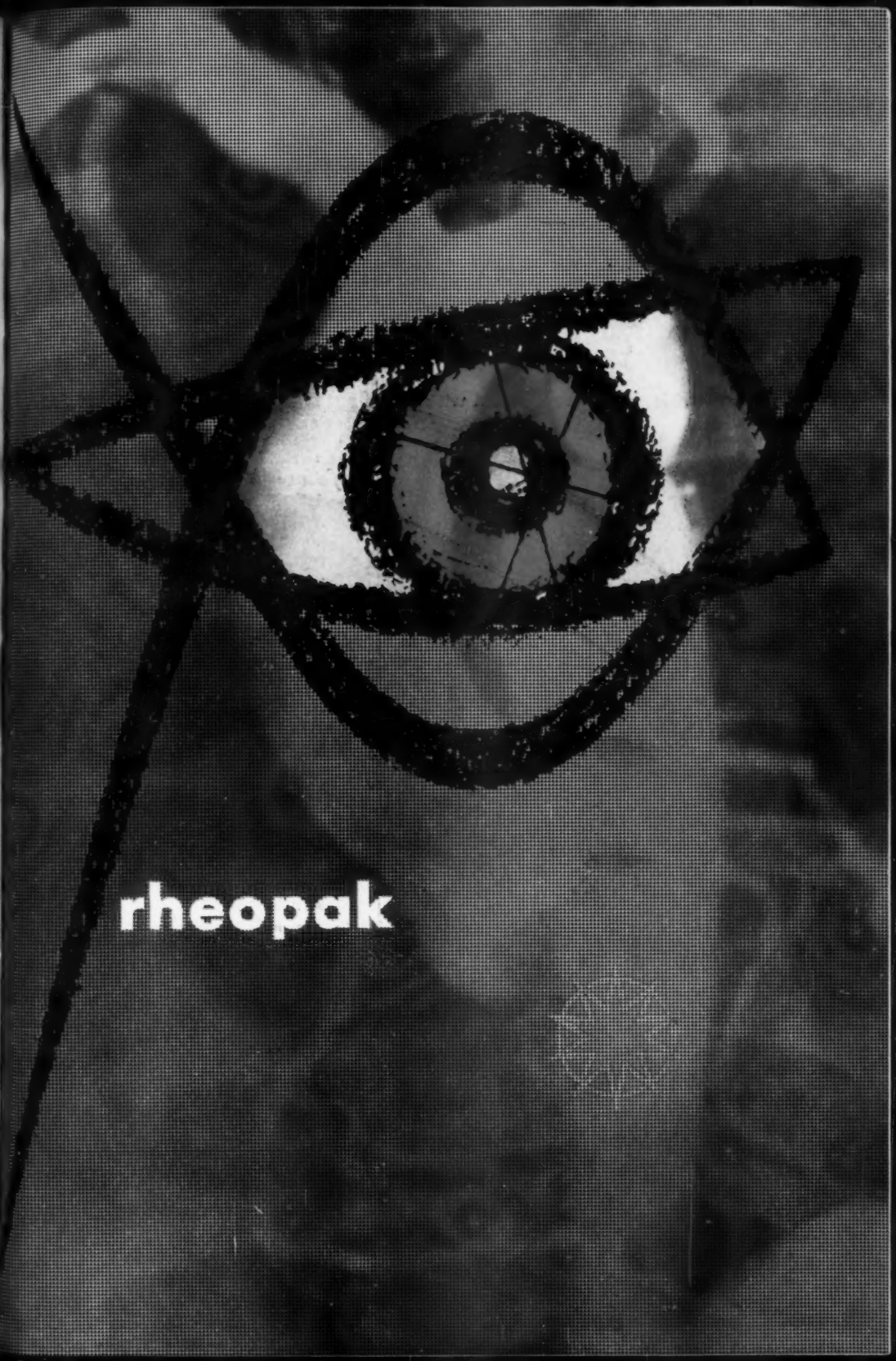
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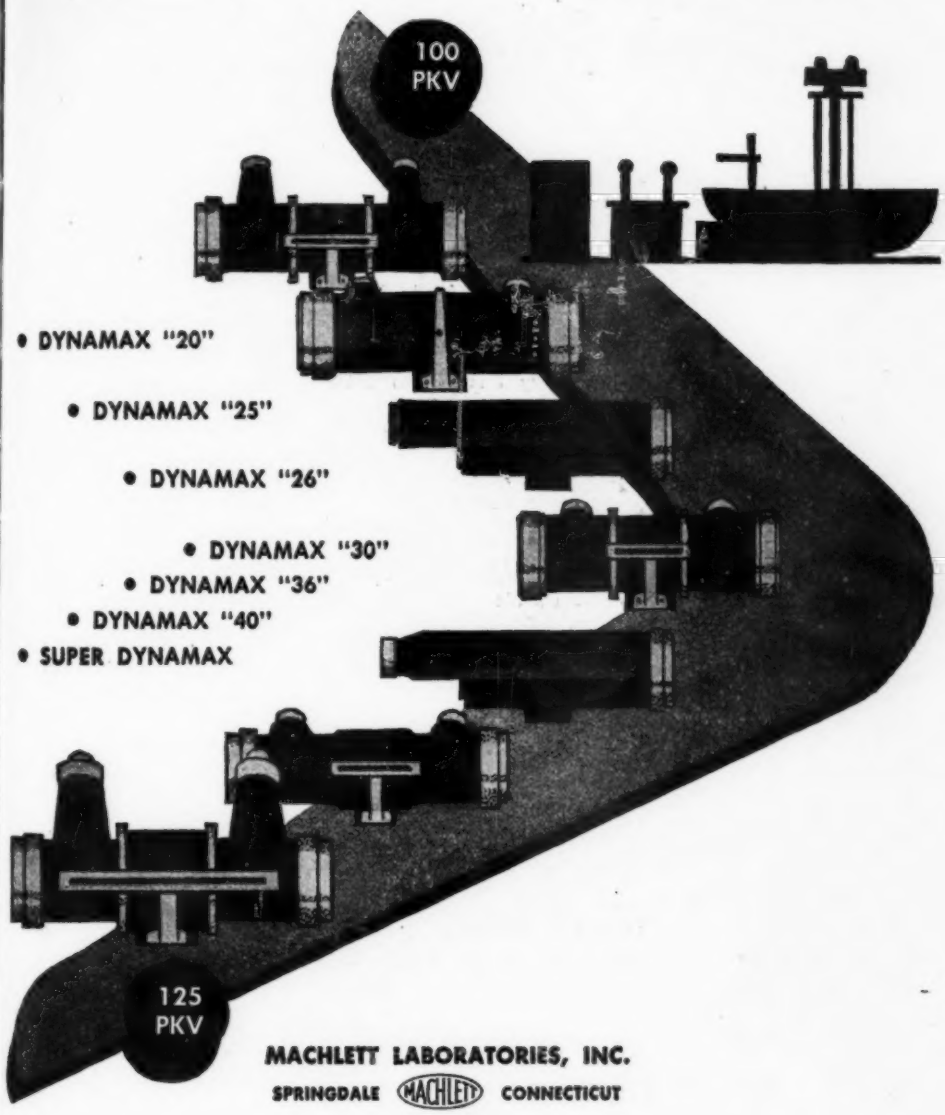

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